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13. ABSTRACT (Maximum 200 Words)

Soft tissue properties represent a major and significant unknown in the domain of medical modeling and simulation. This program presents a 4-year research effort in defining tissue characteristics of three distinct organs (liver, spleen, and kidney) *in vivo*.
Over the course of this program, we will use novel methods of tissue interrogation to characterize non-linear behavior during slow deformations, as would commonly be seen during surgical manipulations. We will then develop mathematical models that can be optimized to permit near real-time representations of organ behaviors, including the boundary characteristics of organs *in situ*.
In year two we developed an *in vitro* experimental setup to approximate *in vivo* conditions; revised year one's testing instruments; devised a new large external indentation device for creep measurements; tested perfused porcine livers using these instruments; investigated a non-invasive technology for determining vessel characteristics; and began incorporating our results into finite element models. Collaborative efforts have allowed us to explore 3D real-time ultrasound as a means of investigating tissue mechanics; compare noninvasive forms of tissue property measurements (harmonic elastography) with our measurements; design a vocal fold tissue property measuring device; and develop a new optical testing modality that can later be used for whole organ validation.

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Table of Contents

Introduction

Computer-based medical modeling and simulation offers the potential for a completely new way to learn medical care. The use of computers as human assistants for medical diagnosis and training will require new knowledge domains. The most fundamental among these is the digital characterization of biophysical properties of perfused organs obtained from *in vivo* measurements, accounting for tissue properties integral to the organ as well as boundary conditions which affect the organ's global behavior.

Our research program is designed to obtain non-destructive measurements of living tissue–liver, spleen and kidney–from large animal models and to use this data to characterize non-linear behavior during large-scale deformations, as would be seen in clinical practice. We are designing instruments to measure tissue properties and then creating mathematical models to allow representation of these data in a computer simulation.

During the second year of research, we have refined our testing instrumentation based on what we learned in year one and devised an experimental set-up that allows us to test our instruments in near *in vivo* conditions. We have made both small and large strain deformation measurements using external indentation and internal compression devices. We explored non-invasive material property probing methods such as tactile imaging for obtaining vessel data and harmonic elastography for bulk material property information. Lastly, through collaborations with other labs the design of a new device to measure larynx material properties, utilization of a 3D real time ultrasound device for internal material property measurements, and a new optical testing modality for future whole organ property validation are underway and opening channels for additional funding.

All work has been done according to institutional- and Defense Department-approved animal studies protocols.

Body

The following sections present our second year results organized according to the Statement of Work from our original research proposal. The points in that Statement include:

- Design vascular tissue property testing device
- Investigate and establish imaging alternatives with attention to representation of boundary conditions from surrounding structures
- Implanted device *in vivo* whole organ tests in animals
- Indentation testing and uniaxial tension testing of component tissues: capsule, vessels
- Perform initial FEM models based on above data

In addition to the aforementioned points, the following were also commenced or accomplished:

- Initial comparisons of indentation testing and harmonic elastography on porcine tissues *in vitro*
- Establishing a relationship with a Massachusetts Institute of Technology (MIT) specialist in soft tissue modeling

- Employing the TeMPeST (Tissue Material Property Sampling Tool) indentation device to examine laryngeal tissues including vocal cords *in vitro*, and establishing a collaboration with the Massachusetts Eye and Ear Infirmary (MEEI) to develop further instrumentation
- Developing of an experimental set-up which allows *in vitro* perfusion of the liver to near physiologic conditions

Design vascular tissue property testing device

Tactile imaging uses an array of passive pressure sensors which, when scanned over the surface of tissue of interest, generate a pressure map that is related to the stiffness of the underlying tissue. Tactile imaging has to date been used to image areas of increased stiffness in tissue, such as cancers in the breast. Vessels in solid organs such as the liver, however, are large enough to register as an area of decreased stiffness under tactile imaging, so we have designed a tactile imaging system for measuring the properties of vessels in porcine and human liver.

The initial tactile imagers have been built for *in vitro* measurements, with an active area of 3.2 cm x 3.2 cm. This allows for a greater surface area to be imaged in order to test our vessel property estimation algorithm. Figure 1 shows the tactile imager built for this study. An array of capacitive pressure sensors is mounted to the smooth aluminum lower surface, and a magnetic tracker, which enables localizing the tactile image in three dimensions, to the handle.

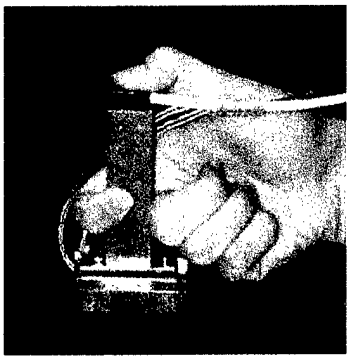

Figure 1: Tactile Imaging Scanhead designed for ex-vivo measurements of liver vessel properties. The aluminum body does not interfere with the magnetic position tracker at the base of the handle (black box). The radius of curvature (into the image) of the scanhead used depends on the type of tissue to be recorded.

Investigate and establish imaging alternatives with attention to representation of boundary conditions from surrounding structures

3D real-time ultrasonic imaging

We have acquired access to technology to perform 3D real-time ultrasonic imaging using a Philips system. Initial work has begun, using the system for tissue mechanics. More specifically, we are investigating the utility of the system to measure 3D displacement fields using a speckle tracking method. Ideally the technology will also be used to identify internal structures (such as vessels, ligaments, etc.) allowing for accurate placement of the internal testing devices into homogeneous regions used for the parenchymal tissue measurements.

Validate harmonic elastography

In October, 2002, two of our investigators, Amy Kerdok and Mark Ottensmeyer, attended the First Annual Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, in Niagara Falls, Canada. There we made contact with researchers investigating non-invasive techniques for extracting tissue stiffness, including ultrasound and magnetic resonance "elastography." These techniques typically impose external deformations or vibrations on the external surface of an anatomical structure (e.g. breast or abdomen), and record the internal geometric changes of tissues. By either comparing "before and after" images, or examining the vibration patterns within the tissue, global images of the "strain field," relative changes in shape of the tissues can be determined. Since the amount of shape change depends on tissue elasticity (i.e. harder tissue deforms less than softer tissue), estimates of the same sorts of material properties of interest to us can be determined. Some of these techniques are in early clinical use, but are more qualitative than quantitative, allowing practitioners to identify areas of local stiffness but not the true, absolute values of elasticity with great precision.

Since non-invasive techniques for elasticity determination would be useful for our eventual measurement of human tissues, and because of the elastography community's interest in validating their techniques, we began a collaboration with Dr. Elisa Konofagou (Harvard Medical School), who is employing a technique called harmonic elastography. Her interest involves creating lesions within tissue using focused ultrasound techniques, then locating and evaluating the lesions by vibrating the tissues internally using lower energy ultrasound beams. We have examined porcine muscle, liver and fat samples using both harmonic elastography and the TeMPeST instrument, looking at normal tissue *in vitro* as well as the lesions to study the changes in local compliance. A schematic illustrating harmonic elastography (Figure 2) and typical results from the TeMPeST and harmonic elastography system are shown (Figure 3).

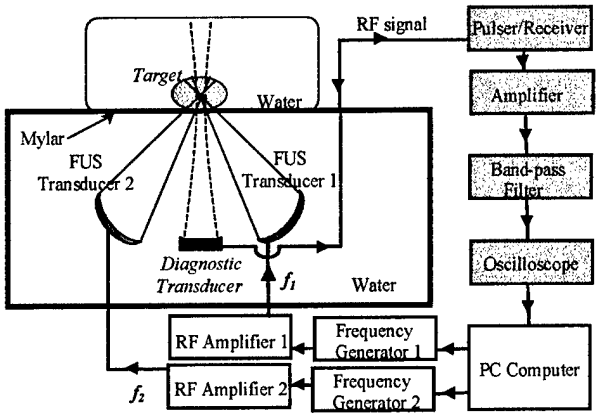

Figure 2: Harmonic elastography schematic. Focused Ultrasound Transducers create lesion in tissue and/or cause small amplitude vibrations. Motion is detected with diagnostic transducer. Amplitude of motion varies inversely with tissue stiffness. (From Konofagou et al., 2003—see Reportable Outcomes)

Implanted device *in vivo* whole organ tests in animals

New experimental set-up: motorized T-needles and perfusion apparatus

A proof-of-concept prototype of a device was developed in year 1 that enters an arbitrary volume of interest and measures the force displacement response of parenchymal tissue between two cylindrical bars. Because this device was manually driven, the true viscoelastic behavior of

the soft tissue could not be obtained. Efforts for year 2 went into motorizing this device so that fast step displacements and varied strain rates could be applied, allowing us to capture the time response of the tissue. Other design optimizations were incorporated to reduce stress concentrations and allow for use on whole organs.

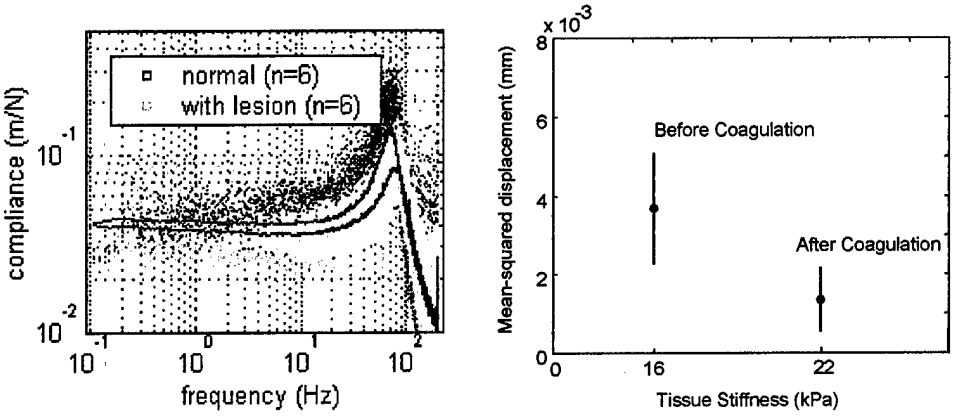

Figure 3: (left) TeMPeST measurement of tissue compliance. Untreated tissue is softer (higher compliance) than tissue with lesion. (right) Measured displacement is larger in uncoagulated tissue. (From Konofagou et al., 2003)

Another lesson learned from year one was that testing *ex vivo* tissues cut to known geometries were far from ideal. Due to the liver's extremely vascular structure and the absence of normal boundaries, fluid escaped during testing, leading to a highly viscous response. The very critical fluid motion variable could neither be controlled nor ignored in a typical *in vitro* environment, thus measurements made on cut tissues were difficult to repeat.

To approximate near *in vivo* conditions, we developed a new experimental setup that incorporated a perfusion apparatus. Using simple hydrostatic pressure principals and the knowledge of liver anatomy and physiology, the apparatus delivers a constant, nonpulsatile flow of Lactated Ringer's solution to the liver via the hepatic artery (120 mm Hg) and portal vein (20 mmHg). The setup consists of using basins as reservoirs suspended from varied heights to set the perfusion pressure, and tubing that matches the diameters of the portal vein and hepatic artery lumen to set the flow rates. The Lactated Ringer's solution is allowed to freely exit the organ via the hepatic vein into a bath, held at 36°C by an immersion heater, and pumped back to the two reservoirs (see Figure 4).

The new set-up and the motorized T-needles were used to test both unperfused and perfused whole porcine livers. To test loading rate dependencies, the tissue was compressed at different ramp speeds, and then the force response was measured over time to determine the relaxation time constants (see Figure 5). The details of these tests are described in [see Appendix A- Kerdok & Howe ASME 2003]. The results demonstrate differences between the perfused and unperfused organ and provide clearer insights into the viscoelastic behavior of the liver.

Despite the success of these experiments, uncertainties in the boundary conditions of the implanted device (variations in strain levels within the test volume due to the bar geometry, assuring proper alignment within the tissue, etc.) make it extremely difficult to interpret the data in a meaningful way. Performing the initial inverse finite element (FE) modeling of these tests to realize the constitutive law requires us to both fully understand the boundary conditions, and to be able to fit a basic law to the data as a starting point for our modeling. Before continuing on

with this more difficult case, we decided it was worthwhile to take a step back and perform some basic large deformation indentation tests on perfused organs using well characterized boundary conditions and obtaining repeatable data sets from which a basic law can be fit. An explanation of the device we built and the tests performed are presented under the next topic.

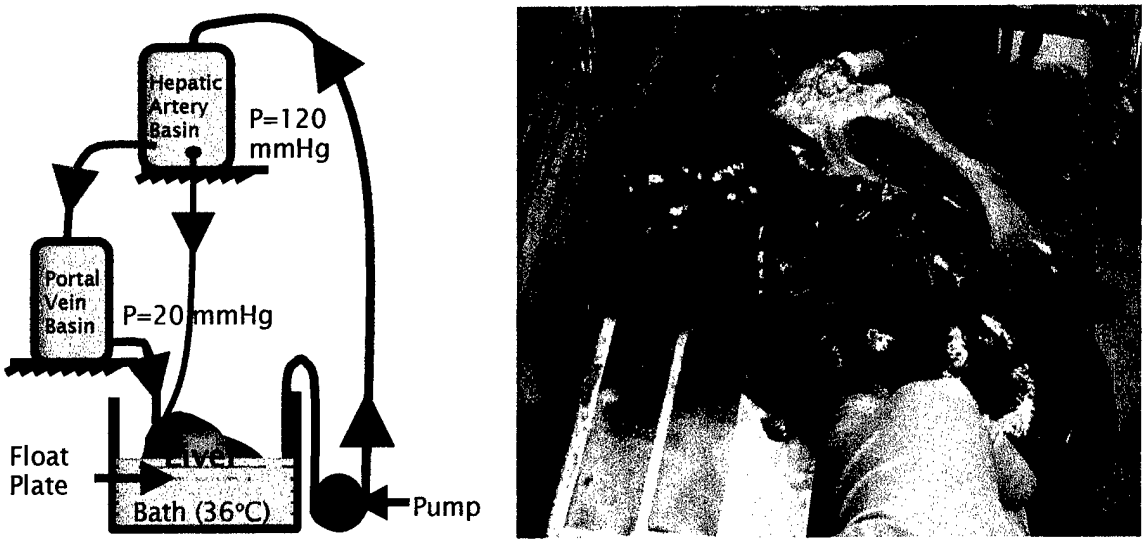

Figure 4: (left) A schematic of the perfusion apparatus depicting the flow path and pressures of Lactated Ringer's solution through a liver. (right) A photo of a porcine liver hooked up to the perfusion apparatus demonstrating flow through a sliced lobe.

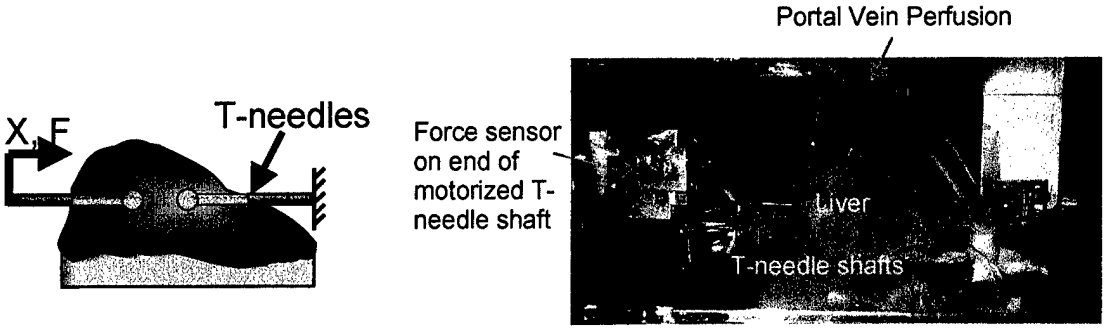

Figure 5: (left) Schematic of T-needles within whole organ on float plate. (right) Photo of test set-up for stress relaxation tests on whole liver using the perfusion apparatus and motorized T-needles.

Indentation testing and uniaxial tension testing of component tissues: capsule, vessels

Manual indentation device and testing

To prove the concept that a controlled large deformation indentation over long periods on perfused whole organs would give us repeatable measurements and insight into the role that fluid plays in the basic constitutive law of liver, we developed a manual creep indenter. The instrument consists of a lever arm with a bucket for weights above a ¼" flat bottom cylindrical indenter, and a potentiometer that measures the displacement of the arm (see Figure 6). The protocol consisted of applying a load as quickly as possible and then recording the change in displacement over time on both perfused and unperfused whole porcine livers. We also made measurements with the TeMPeST device in the same three locations on both of the livers tested. A summary of the results for both devices is discussed below.

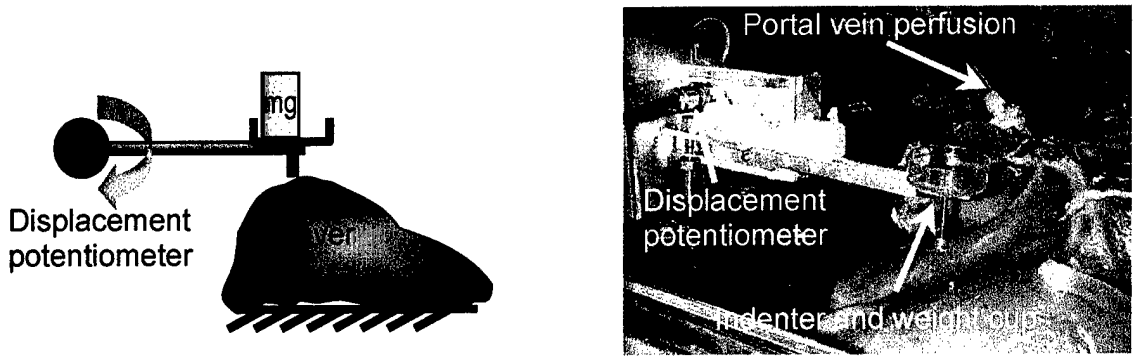

Figure 6: (left) Schematic of manual creep setup. (right) Photograph of indenter arm sitting level on a perfused porcine liver.

Manual creep indenter and TeMPeST test results

Basic indentation measurements were made using both the manual creep indenter (large constant strain (10-90%) with step loads (6.3-62 kPa)) and the TeMPeST indenter (small sinusoidal strains applied at 0-200 Hz) on the same locations of perfused and unperfused porcine livers *in vitro.*

The manual creep device on the perfused organs resulted in very repeatable measurements (both within and across organs) with a clear viscoelastic response (see Figure 7). Differences between perfused and unperfused tissue response over time supports the need for employing a perfusion apparatus that approximates near *in vivo* conditions. Similarly, the differences in compliance measured with the TeMPeST (see Figure 8) provide independent confirmation of differences due to state of perfusion. The results clearly indicate that without perfusion the tissue loses its viscoelastic response over time and shows a stiffer response.

Fung's quasilinear viscoelastic theory was chosen as the initial model to which to fit the creep data, using a simplex method. Although not suited for finite strains, the popularity of this theory and its ability to help us understand the time response of the tissue made it a natural choice for our first approximation. The results indicate that there are 4 loading time constants (see Equation 1) ranging from 200 ms to 200 sec. The weighting terms, "c_i," suggest that the smallest time constant is the most important. These time constants did not change across varying loads. Due to the fact that this data was collected on an indenter whose loads were manually applied, the 200ms time constant (the most significant one) lies very close to the limits of the test. However, despite the tests limitations, it revealed that taking a step back and performing basic controlled indentation testing is a truly worthwhile endeavor. Modifications to the existing setup that will allow for a more complete and accurate data set to be collected are described in the conclusions section.

$$\sigma(\varepsilon,t) = G(t) * \sigma^{e}(\varepsilon)$$

$$G(t) = c_0 + c_1 e^{-\tau_1 t} + c_2 e^{-\tau_2 t} + c_3 e^{-\tau_3 t} + c_4 e^{-\tau_4 t}$$

$$= 1 - 0.09e^{-242.39t} - 0.14e^{-23.7t} - 0.24e^{-2.89t} - 0.62e^{-0.21t}$$

Equation 1: Quasilinear viscoelastic model. Stress (σ) is a convolution of a function of time, G(t), and a time-independent, non-linear function of applied strain, $\sigma^e(\varepsilon)$. A model with four time dependent terms is found to have a good fit to the data. The weights of each term show that the shorter time constant terms dominate the description of the response. In this formulation, all of the weights are normalized to c_0.

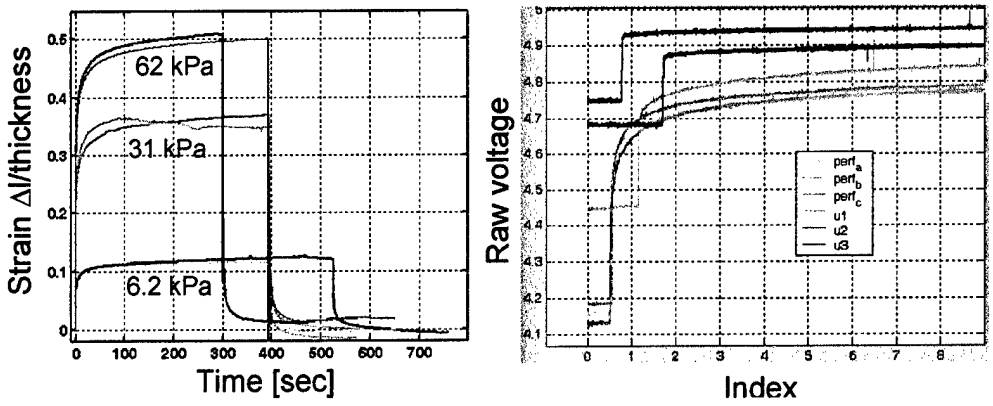

Figure 7: (left) Manual creep indentation data from the second liver in first test location (27.5 mm thick). Note the repeatability in the data as two measurements were made at each strain state. (right) A close-up of the raw data for the 31 kPa loading state on the first liver in both the perfused (yellow, pink, red) and unperfused (light blue, blue, black) over time. Note the repeatability and smooth curve of the perfused data versus the non-repeatable stiffer unperfused data. The differences in the starting voltage is a result of the unperfused liver being thinner than the perfused liver, and that indentations made on the unperfused organ did not recover after the load was removed, and thus reset the zero point for subsequent indentations.

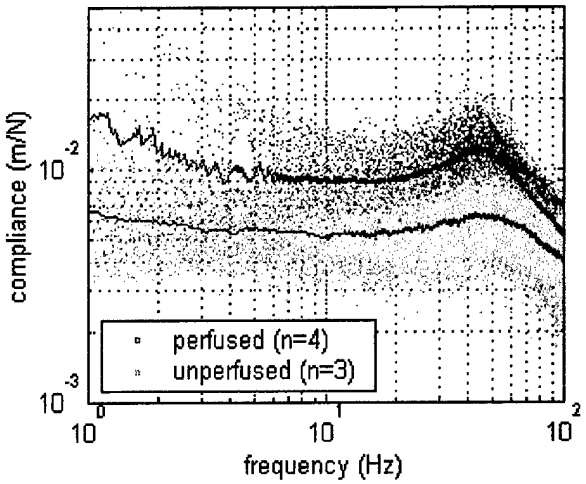

Figure 8: TeMPeST compliance measurements of perfused and unperfused liver. Stiffness differs by approximately a factor of two.

TeMPeST modifications

Two significant upgrades were made to the TeMPeST instrument to reduce the temperature sensitivity of the force sensor and to enable comparison of our results with a wider range of published data.

Temperature sensitivity is a drawback of silicon strain gauges, including those used in the TeMPeST force sensor. In the original design, this factor was not considered, and as a result, early *in vivo* tests performed laparoscopically were subject to drift in the force signal, which made measurement of the mean value of force unreliable (although higher frequency results were unaffected). To reduce temperature effects, the force signal excitation was changed from a

constant voltage source to a constant current source. We designed a printed circuit board to include both kinds of sources, in case there were circumstances that required returning to the original configuration.

The second modification reflects the use of hemispherical indenters by various research groups to measure tissue compliance. We redesigned and rebuilt the force sensor itself to easily switch between flat cylindrical and hemispherical indenter tips. No experiments using the hemispherical tip were conducted in year two, although they have been considered as this geometry does not cause the stress concentrations that the flat indenter generates around its relatively sharp edge.

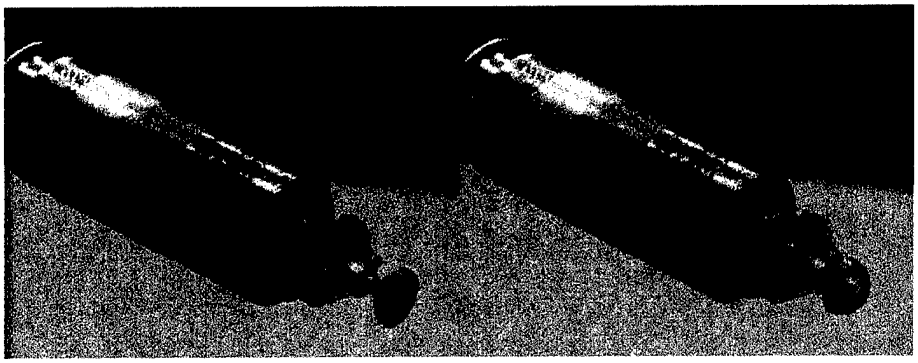

Figure 9: TeMPeST indenter with flat circular (left) and hemispherical (right) contact tips. Both are 5mm diameter.

Perform initial FEM models based on above data

Vessel data

From the tactile imaging vessel data, thirty-six finite element models of hollow vessels embedded in soft tissue were analyzed using Abaqus Standard 5.8.1 (HKS Inc. Pawtucket RI). An example model is shown in Figure 10. The tissue thickness was varied from 40 to 60 mm and the vessel diameter from 5 to 10 mm. Surface pressure profiles are recorded every 2mm, corresponding to the expected rate of *in vitro* data collection (10Hz, 20mm/s). The tactile information gathered is independent of the vessel pressure for pressures at or less than the physiological liver vein pressures.

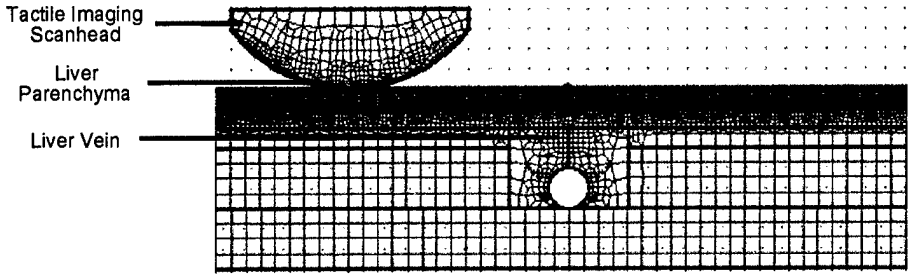

Figure 10: Finite element model of liver parenchyma with embedded vessel. The vessel can be modeled as empty, or full of pressurized liquid. In our simulations, the scanhead is indented into the tissue at left and scanned along the surface of the tissue. Surface pressure values are recorded to simulate tactile imaging.

The tactile information is inserted into an inversion algorithm [see Appendix A, Galea 02] so that the tissue and vessel parameters of interest are estimated. The results of estimating

the model tissue and vessel parameters are shown in Figure 11 and summarized in Table 1. The estimation of the parameters of interest shows small errors, and is promising for application to real data.

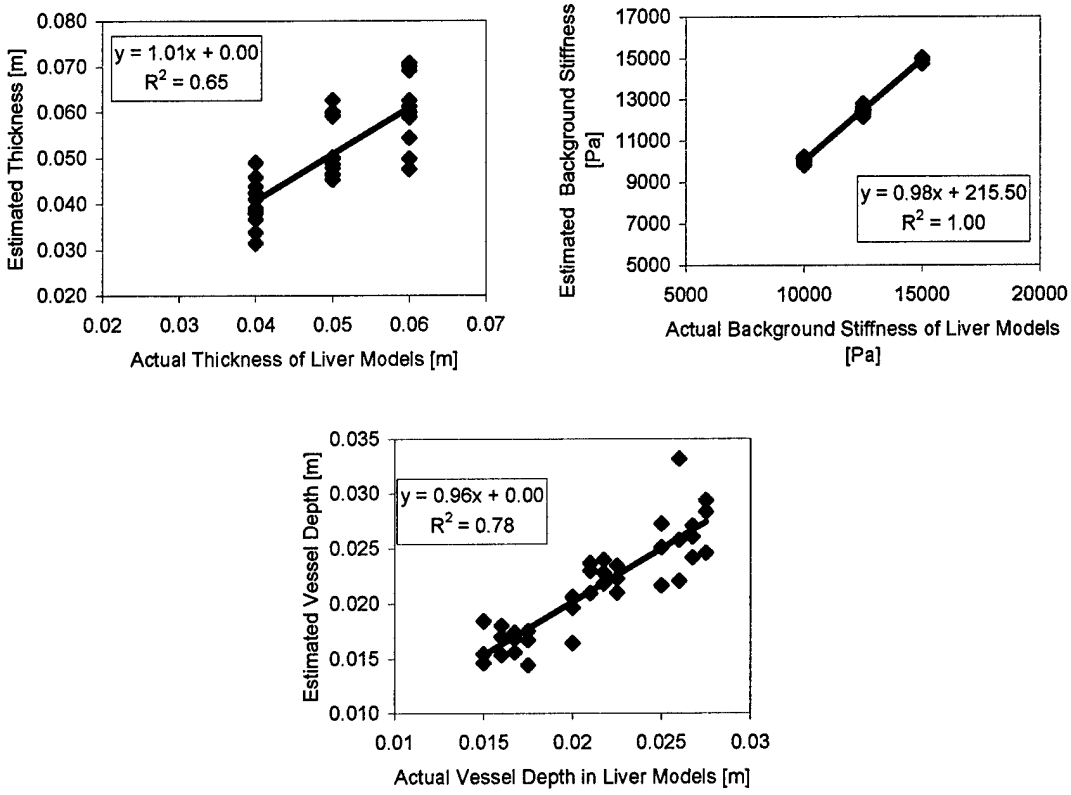

Figure 11: Estimating underlying parameters from finite element models of livers with embedded vessels.

Table 1: Mean Absolute Error in estimating the underlying parameters of liver finite element models.

Parameter	**Mean Absolute Error in Estimation**
Liver Modulus B	0.81%
Liver Thickness t	9.3%
Vessel Depth z	7.2%

Indentation data

As mentioned above, modeling the T-needle data was not readily feasible so we reconsidered a simpler technique to collect data with more controlled boundary conditions. From the manual creep indentation data mentioned above, we were able to obtain clean, repeatable measurements that have allowed us to begin our FEM work. We have been working with a colleague whose work focuses on modeling cervical tissue. After consulting with her, it has become apparent that the data we have collected fits well with her model. The model consists of

nonlinear elastic springs representing the collagen network in the tissue, a damper representing the interstitial fluid, a spring to act as the initial response to overcome the ground substance, and a damper to represent the shear response of the parenchymal cells. Work has begun on incorporating our results into her model, and we hope to have a model of indenting parenchyma (perhaps even with capsule) early next year. The model in question awaits publication, and as a courtesy, we will hold further details regarding this collaboration for next year's annual report.

Additional endeavors

Vocal fold testing

The Voice Restoration Group (VRG) at the Massachusetts Eye and Ear Infirmary (MEEI) approached our group to help define the mechanical properties of tissues in the human larynx, especially the vocal folds. If damaged from disease or overuse, the vocal folds will not vibrate normally, preventing the normal production of a speaking or singing voice. Because vocal communication is so critical to economic performance and normal human interaction, this can be a critical disability.

A novel and promising treatment approach is to implant or inject a bio-compatible gel material with the same visco-elastic properties as the healthy superficial lamina propria (SLP), the gel-like layer that vibrates during speaking or singing. To identify and design the best bio-material, the mechanical properties of healthy tissues must be determined. Furthermore, an intra-operative method for verifying that the implant behaves correctly would help to avoid unsuccessful surgery.

Towards these goals, the TeMPeST instrument was used to measure the compliance of bovine, ovine and human cadaver larynx tissue samples. An *in vitro* test and examples of early results are shown in Figure 12. We have shown that vocal fold SLP tissue can be easily distinguished from the arytenoid cartilage (one of the anchoring points for the vocal cord). The experiments also clearly showed that the 5mm indenter tip of the TeMPeST was too large for measuring structures that are typically 20mm long, approximately 5mm wide, and typically only 1.5mm thick. Because of this, we have entered into a collaboration to develop instrumentation designed specifically for these anatomical structures. In the initial phase of this work, a "benchtop" instrument has been designed for tissue testing *in vitro*. This instrument will serve also to guide development of a surgical instrument, which will be developed in a future phase of the research.

As measurement of vocal tissues falls outside of the original scope of our work on solid organ tissues, the VRG is providing funding for the work beyond the initial tests using the TeMPeST instrument. However, if it should prove a promising measurement technique, the new instrument may be used on solid organ tissues as well.

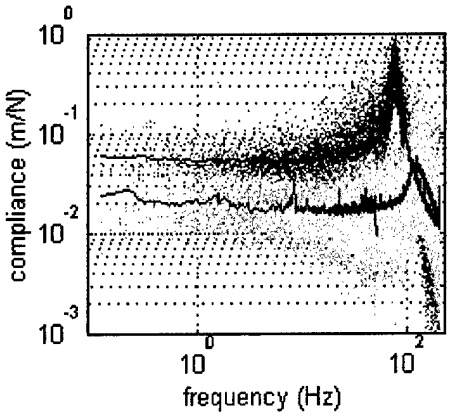

Figure 12: (left) TeMPeST used to test bovine larynx and (right) compliance of vocal fold (dark) and cartilaginous vocal process (light)

Development of optical imaging-based testing technique

During this past summer, we had the unique opportunity to host a high school physics teacher and help her develop a project that was simple enough to bring back to high school students and perform on a limited public school budget. The project we devised investigated whether we could obtain material property information from solid organ tissue by applying a simple deformation and analyzing digital images of the shape of a soft tissue's surface (see Figure 13). The goal was to develop a material testing apparatus to induce a plane strain state on the material using knife-edge indentation and then to visually inspect the surface response. Work on the gel phantoms was promising enough that we will continue this work to provide another testing modality for future whole organ validation.

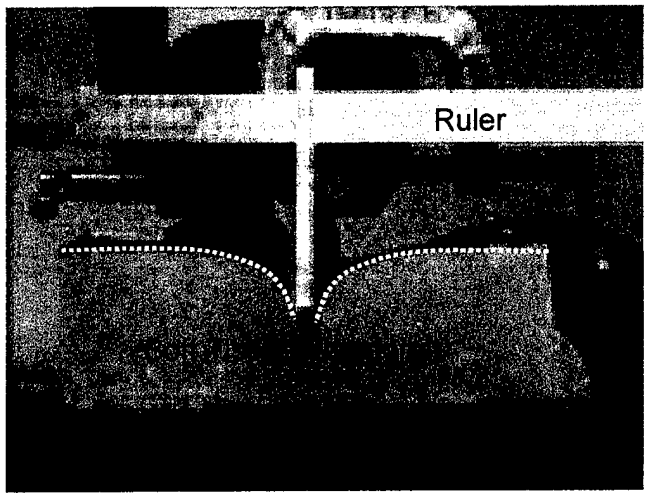

Figure 13: Image captured from video system of "knife edge" causing plane strain (i.e. no "out of the page motion") in silicone gel tissue phantom.

Key Research Accomplishments

- Utilized a tactile imaging device to obtain porcine liver vascular data *in vitro*
- Conducted tests comparing harmonic elastography with TeMPeST compliance tests

- Explored the use of 3D real-time ultrasound for measuring tissue properties, boundary conditions, and as a guide for placement of the parenchymal testing device
- Made revisions to T-needles and TeMPeST as was indicated from year one results
- Developed a perfusion apparatus to approximate *in vivo* conditions for *in vitro* experiments
- Developed large strain manual creep indentation device
- Made measurements on perfused whole porcine livers using both the TeMPeST and manual creep indentation device
- Developed FE models of tactile scanning of liver with vessels
- Began to incorporate acquired creep data into a nonlinear, physically-based soft tissue constitutive model
- Made initial tests on vocal tissues with TeMPeST
- Defined a new optical testing modality for use in future whole organ model validation

Reportable Outcomes

Journal papers

- A.E. Kerdok, S.M. Cotin, M.P. Ottensmeyer, A. M Galea, R.D. Howe, and S.L. Dawson, "Truth Cube: Establishing Physical Standards for Real Time Soft Tissue Simulation," Medical Image Analysis, vol. 7, pp. 283-291, 2003.

Conference papers

- D. Kalanovic, M.P. Ottensmeyer, J. Gross, G. Buess, S.L. Dawson, "Independent testing of soft tissue viscoelasticity using indentation and rotary shear deformations," MMVR11. Proceedings of Medicine Meets Virtual Reality 11, Newport Beach, CA. IOS Press. pp137-143. 22-25 Jan 2002.
- E.E. Konofagou, M.P. Ottensmeyer, S. Agabian, S.L. Dawson, K. Hynynen. "Estimating localized oscillatory tissue motion for assessment of the underlying mechanical modulus," IEEE Ultrasonics, Ferroelectrics and Frequency Control Symposium, Honolulu, HI, Oct. 5-9, 2003, in press.

Invited lectures/workshops/meetings

- A.E. Kerdok, R.D. Howe: "Measuring Parenchymal Properties of Perfused Solid Organs", MIT Health Sciences and Technology 2003 Forum Abstract
- A.E. Kerdok and R. D. Howe, "A Technique for Measuring Mechanical Properties of Perfused Solid Organs," presented at ASME Summer Bioengineering Conference, Key Biscayne, FL, 2003.
- M.P. Ottensmeyer, "In vivo measurement of the mechanical properties of soft tissues." City College of New York, Biomedical Engineering Seminar Series, 15 April 2003.
- M.P. Ottensmeyer, "Measuring properties of living tissue or How to make Virtual Organs feel right." Virtual Medicine and Cybercare, course code ENGS013, Thayer School of Engineering, Dartmouth College, 29 July 2003.

Conclusions

The second year's efforts led to progress in our stated goals, a number of new opportunities which were not foreseen at the outset of the research program, and some lessons learned and alternate approaches where the original directions proved less fruitful that expected.

We have expanded our suite of testing techniques to include a new large strain indentation device, a tactile array probe useful for gathering data on large vessels non-invasively, an optical technique for extracting large strain deformation data, and an ultrasound-based technique to investigate tissue properties non-invasively. In addition, the perfusion system developed this year allows us now to keep organs in a much closer to living state than previously, including maintaining hydration, temperature, physiologic pressure, and osmotic balance through the use of heparinized Ringer's solution.

Acquiring data directly on parenchymal tissue using the T-needle system proved difficult because of the complexity of ensuring that the boundary conditions were the same in each test (i.e. exact placement of the needles). Re-examining well controlled large strain responses of whole organs in a perfused state by using the manual creep indenter and perfusion set-up proved to be a worthwhile task. The results of these experiments support the need to continue work on these more controlled experiments before returning to the internal devices (T-needles). Thus we are motorizing the large strain indenter setup to permit controlled step loading (to measure the creep response), step displacements (to measure the stress relaxation response), and varying strain rates to provide us with the information necessary to accurately analyze the tissue's response. In addition to performing more tests to increase the robustness of our data sets, another goal is to obtain data *in vivo* using both the creep and TeMPeST devices and perfused *in vitro* data to study changes between tissue *in vivo* and the same tissue supported by the perfusion system.

One of our goals it to determine capsule properties. By performing tests on areas of the perfused organ where we remove the capsule, and comparing this data to previously collected intact data, the differences in the response will be due to the contribution of the capsule alone. Such tests will be expanded during year three.

Work has begun to investigate a new means of probing the parenchyma internally using hepatic vein balloons normally used to measure hepatic pressure (see Figure 14). It is likely that after the indenter data is collected, these balloons will be our next step towards obtaining internal data due to their less invasive deployment, and more controlled boundary conditions. Essentially, modified balloon catheters can be positioned endovascularly within the liver and expanded, while measuring the pressure applied and the balloon volume. These data are analogous to the force and displacement data acquired during indentation or T-needle testing. Since placement of such balloons is already established for human surgery, such a technique may well be among the first techniques we apply to measuring human organ properties.

The balloon catheter device may also make determination of vascular properties possible. From our observations during dissection of porcine liver, to a reasonable approximation, the hepatic vein is an endothelial cell lined cavity, while the hepatic portal vein has a tougher lining. Since both are surrounded by liver parenchyma, the difference in the pressure-volume response will be dominated by the presence or absence of the vessel lining, and as with the capsule testing, will lead to data to quantify the lining's properties.

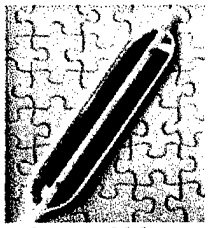

Figure 14: Example of a dilation catheter balloon that could be used to probe parenchymal properties (photo courtesy of NuMED http://www.numed.on.ca/nubackground.htm)

"So what?"

The knowledge gained in the second year of this program continues the establishment of a path toward *in vivo* characterization of solid organ tissue behavior during clinically relevant manipulations. This information will be crucial to creation of effective medical training systems that can be designed to reproduce biological properties without requiring, for example, the use of animals for training. Although medical simulation holds much promise for changing the way medical knowledge has been imparted for millennia, truly effective learning of what to expect, how to react, and how to correct errors is the essence of medical wisdom. Without biological properties, computer graphics are just cartoons, devoid of relevance to patient care. But with biologically accurate behavior, computer simulations can become a replacement for learning on humans and animals. This work explores several pathways to obtain the biological data in as less invasive and most natural way as is possible to enable this transition.

Appendix A: Papers, Abstracts, Supporting Material

Kalanovic et al., 2003

D. Kalanovic, M.P. Ottensmeyer, J. Gross, G. Buess, S.L. Dawson, "Independent testing of soft tissue viscoelasticity using indentation and rotary shear deformations," MMVR11. Proceedings of Medicine Meets Virtual Reality 11, Newport Beach, CA. IOS Press. pp137-143. 22-25 Jan 2003.

Kerdok & Howe, 2003

A.E. Kerdok, R.D. Howe: "Measuring Parenchymal Properties of Perfused Solid Organs", MIT Health Sciences and Technology 2003 Forum Abstract

Kerdok & Howe, 2003

A.E. Kerdok and R.D. Howe, "A Technique for Measuring Mechanical Properties of Perfused Solid Organs," presented at ASME Summer Bioengineering Conference, Key Biscayne, FL, 2003.

Kerdok et al., 2003

A.E. Kerdok, S.M. Cotin, M.P. Ottensmeyer, A.M Galea, R.D. Howe, and S.L. Dawson, "Truth Cube: Establishing Physical Standards for Real Time Soft Tissue Simulation," *Medical Image Analysis*, vol. 7, pp. 283-291, 2003.

Medicine Meets Virtual Reality 11
J.D. Westwood et al. (Eds.)
IOS Press, 2003

137-143

Independent testing of soft tissue visco-elasticity using indentation and rotary shear deformations

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Numerous techniques exist to measure the mechanical properties of soft tissues *in vivo*, such as mechanical stretching, indentation or shearing, as well as elastographic methods employing ultrasound or other imaging modes. Many groups have reported properties which do not necessarily correspond with each other due to differences in choice of technique, tissue model or other variations. This work deliberately makes use of the two independent modes of indentation and rotary shear, on the same material samples, employing similar modeling approximations, to attempt to determine the common, underlying material properties.

This paper introduces the ROSA-2 rotary shear instrument, and presents its mechanical characteristics, as well as presenting validation experiments that were performed to verify non-slip contact with tissue. Measurements made with it are compared with those acquired with the TeMPeST 1-D indentation instrument. Initial testing showed reasonably agreement when testing silicone gel samples, over a restricted range of frequencies. When testing bovine liver samples *in vitro* and porcine liver *in vivo*, significant discrepancies were found. The potential sources of these differences will be discussed, as will directions for ongoing work.

1. Introduction

The mechanical properties of soft tissues are of increasing interest for medical diagnosis and surgical simulation. In the former case, mechanical testing may aid in deciding whether or not to remove tissue when other tests are inconclusive or inconvenient. In the latter, it is essential that surgical trainees do not learn tasks incorrectly because of shortcomings of the training system. For example, a simulator with tissue stiffness much higher than real tissue could lead trainees to apply excessive forces when they first perform surgery on live patients. For both of these applications, detailed knowledge of the mechanical behavior and properties of living tissue is crucial.

Recently, numerous research groups have been actively developing techniques and instruments for *in vivo* determination of tissue properties. Purely mechanical testing may use indentation probes [1, 2, 3], tension testers [4], compression techniques [5], rotary shear applicators [6] or other deformations. Ultrasound elastography [7] and magnetic resonance elastography [8] combine mechanical deformation and measurement of resulting strain fields to extract elasticity data Results are beginning to become available for *in vivo* tests

(e.g. [1, 4]), but in many cases, the data obtained are not easily comparable, either because the tissue models employed or the testing domains (strain or frequency range) are not comparable, or merely because few tests are done on the same tissues. To begin validating the emerging data, a number of these obstacles must be overcome. The approach described here involves comparison testing of two instruments with independent testing modes on the same tissues, with overlapping ranges of applied strain and strain rates, and subsequent analysis of the results assuming the same constitutive model.

2. Methods and Instrumentation

The TeMPeST 1-D (Tissue Material Property Sampling Tool) indenter and the ROSA-2 Rotary Shear Applicator were used (see Figure 1). The TeMPeST 1-D will be briefly reviewed (see also [3]) and ROSA-2 function, calibration and validation tests will be described.

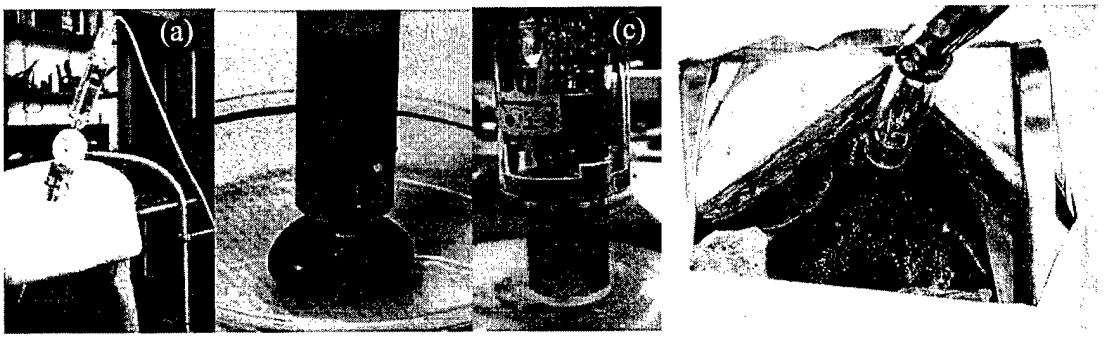

Figure 1: Instrumentation: (a) TeMPeST 1-D instrument passing through 12mm surgical port; (b) detail of indenter deforming rat kidney; (c) ROSA-2 with fixation ring; (d) ROSA-2 testing porcine liver *in vivo*.

2.1 TeMPeST 1-D

TeMPeST 1-D [3, 9] (Figure 1a,b) is a 12mm diameter minimally invasive instrument, designed to measure the compliance of solid organ tissues. A 5mm right circular punch vibrates the tissue while recording applied load and relative displacement. Mechanical bandwidth is approximately 80Hz when in contact with organ tissues; range of motion is 1mm; and forces up to 300mN can be exerted. It has previously measured the properties of porcine liver and spleen *in vivo*, rodent (rat) liver and kidney *in vitro* [10], and has been used in initial investigations of bovine, ovine and human vocal tissue samples *in vitro*.

2.2 ROSA-2

ROSA-2's (Figure 1c,d) 6mm right circular contact rotates relative to a concentric ring fixed to the tissue. Non-slip contact is maintained using a densely packed pin array or a tissue sealant/adhesive. A calibrated galvanometer exerts torque and rotations up to +/-15° are recorded with a non-contact, analog optical sensor with a resolution of ~0.004°. Rotor inertia and friction are smaller than in an earlier version [6], so higher frequency responses can be investigated. A recently implemented closed loop (CL) position controller provides a bandwidth of approximately 20Hz when in contact with materials similar in compliance to solid organ tissue, although it should be possible to extend this range.

Non-slip contact with the tissue is maintained with a densely packed annular array of fine needles (approx. 1500 steel needles of 100μm dia). or a disposable flat acrylic tip to

which a tissue adhesive is applied (see Figure 2). Band-Aid Liquid Bandage (a cyanoacrylate, Johnson & Johnson, Skillman, NJ) was used as the adhesive.

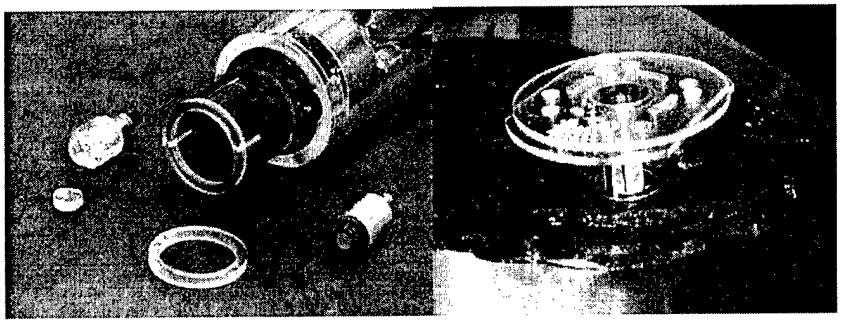

Figure 2: (Left) ROSA-2 rotary shear instrument showing (L to R): flat tip adhesive contact head (with contact tip); fixation ring (with contact ring); and needle array. (Right) *In vitro* test rig for non-slip and damage examination. Note holes in needle array for spinal needle alignment for injection of barium sulfate.

3. Experiments

A series of validation tests were conducted with ROSA-2 to study the non-slip characteristics of the two contact heads, damage-free tissue deformation limits, and finite element analysis (FEA) predictions of the region of influence of torsion testing. Following these tests, comparisons were made between the TeMPeST 1-D and ROSA-2 on silicone gel samples, bovine liver *in vitro*, and porcine liver and spleen *in vivo*.

3.1 Static testing for angular motion limits

A mock-up with the same contact geometry as ROSA-2 was constructed (see Figure 2), which could be used to apply known, fixed rotations to the tissue using either contact head. The mock-up was placed on or bonded to store-bought bovine liver samples, and the heads were rotated incrementally up to angular displacements of 90° for 100 seconds and returned to zero. Visual inspection and histological examination of the tissue was employed to determine the presence of damage and obvious slipping of the contact heads.

3.2 Fluoroscopic testing of region of influence

The contact heads and the static mock up were designed such that a 22-gauge spinal needle could be precisely placed adjacent to the contact zone (see Figure 3), allowing the injection of narrow lines of barium sulfate contrast medium into the parenchyma of the bovine liver tissue. Prepared samples were placed in the imaging field of a Siemens AG (Munich, Germany) Neurostar fluoroscope, and images were generated with rotations up to 90°. These early tests were for qualitative verification of FEA predictions, and to confirm the visual evaluations of slip conditions made previously.

3.3 Silicone gel tests: TeMPeST 1-D vs. ROSA-2

Two different samples[1] of two-part RTV silicone gel 6166 (GE Silicones, Waterford, NY), each 10cm in diameter and 12mm thick, were measured with both the TeMPeST 1-D and ROSA-2. Earlier TeMPeST results [3] were compared with new ROSA-2 tests, performed

[1] 30:70 and 40:60 mixtures of RTV6166 components A and B respectively, by volume. See [3] for additional measurements and comparison with parallel plate rheometry measurements.

under CL control with commanded mean and amplitude angular deformations of 15° and 5° respectively. The frequency range of chirp signal inputs was 0.1 to 100Hz.

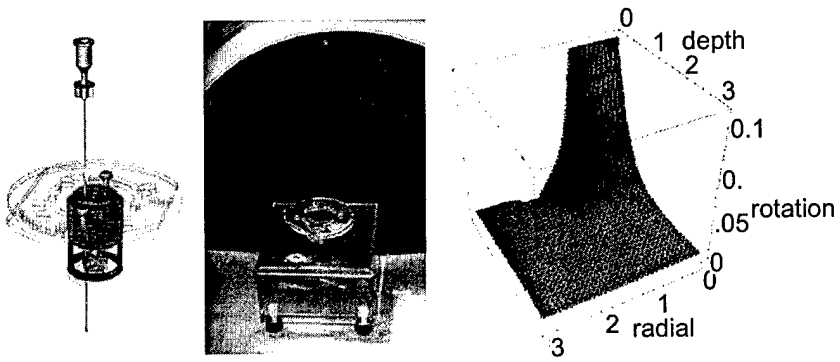

Figure 3: Static test rig showing spinal needle (left) and bovine liver sample in test apparatus in front of fluoroscopy detector (center). FEA model predicting rotation vs. radial position and depth (right)

3.4 *Bovine liver tests* in vitro: *TeMPeST 1-D vs. ROSA-2*

Bovine liver was measured with both instruments under open loop (OL) control at four different locations under the following conditions: ROSA-2 nominal torque preloads and amplitudes of up to 0.15 and 0.21mN·m, and frequencies from 0.0076 to 200Hz; TeMPeST 1-D force preloads and amplitudes of up to 72mN and 84mN, and the same frequencies.

3.5 *Porcine liver and spleen* in vivo: *TeMPeST 1-D vs. ROSA-2*

With appropriate approval, both instruments were tested on porcine liver and spleen *in vivo* (see Figure 1d). As previously described, TeMPeST 1-D testing was performed during 20 sec. periods of suspended ventilation, so that pulmonary action would not overwhelm the small deformations generated during normal indentation. OL force preload and amplitude for the TeMPeST 1-D were 35mN and 42mN respectively. ROSA-2 torque preload and amplitudes were 0.17 and 0.13 mN·m. Rotary action of the instrument relative to the fixed ring was less sensitive to breath motions, so sampling intervals lasted up to 131 sec.

4. Results & Discussion

4.1 *Static testing for angular motion limits*

The histology slides in Figure 4 show the untested surface, a region tested with the needle array and a sample after the adhesive disk had been removed. The needles caused no apparent damage, but removal of the adhesive disk destroyed the capsule, so any damage from testing alone is not apparent. However, since needle array testing caused no damage, adhesive disk damage, prior to removal, is unlikely.

4.2 *Fluoroscopic examination of region of influence*

Fluoroscopic imaging also qualitatively supports early FEA (see Figure 3), which indicates that the region of influence is approximately equal to the radius of the fixation ring. This can be seen in Figure 5, in which the depth of twisting of the barium sulfate lines is of the

same order as the distance between the center of the indenter and the fixation ring. Further, it can be seen that contact is maintained throughout the range of rotation.

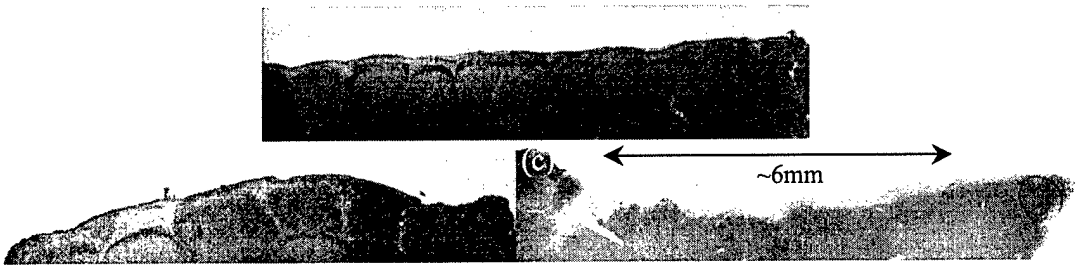

Figure 4: Histology slides of tissue (a) untested, (b) tested with needle array and (c) after removal of adhesive-bonded contact head. No visible damage in (b), but tissue surface is damaged post-removal.

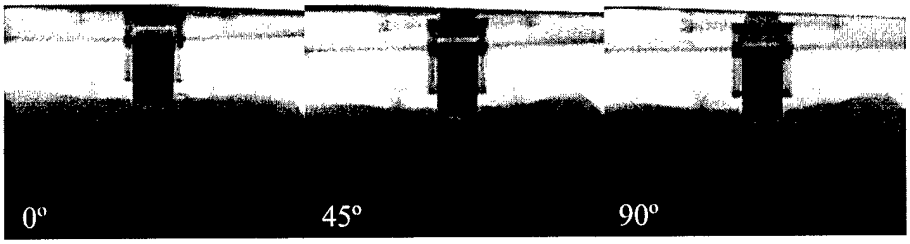

Figure 5: Sequence showing needle array on bovine liver sample. Three injections of barium sulfate visible as needle array is rotated from by 45° increments from 0° to 90°.

4.3 *Silicone gel tests*

Silicone gel tests show good agreement between the two instruments, at least over a restricted range of frequencies (approx. 0.5 to 10Hz, see Figure 6). Assumptions for the simple modeling scheme are: linear (visco-)elasticity, homogeneity, isotropy, incompressibility, small (infinitesimal) deformations and contact with a semi-infinite body. The ROSA-2 data further assume rotation neglecting the fixation ring. With these assumptions, compliance can be converted directly to elastic modulus values [11].

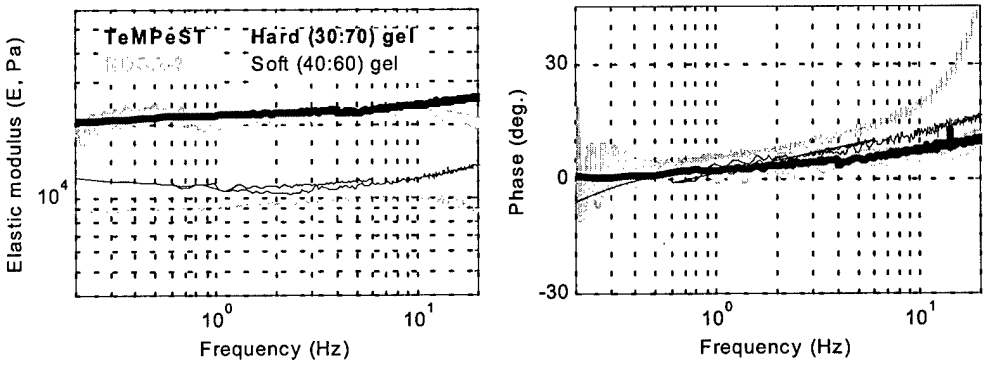

Figure 6: Silicone gel results. Elastic modulus in Pa (left) and phase angle (right).

4.4 *Bovine liver test* in vitro

Figure 7 shows significant discrepancies between the behavior of bovine liver samples as measured by the two instruments. At low frequencies, elastic behavior is observed (i.e. constant modulus and near zero phase angle), confirmed by both instruments. However the source of the nearly two order of magnitude shift in the curves is unclear, especially given the close agreements shown in the gel tests. At higher frequencies, a large contribution is

the inertial effect of the galvanometer, however this cannot account for the low frequency difference. Further analysis and deeper understanding of the measurements and instruments may provide insight to resolve this problem. One possibility is that the ROSA-2 testing reaches higher along the non-linear stress-strain response than TeMPeST 1-D tests. Future experiments will investigate smaller deformations to verify this explanation.

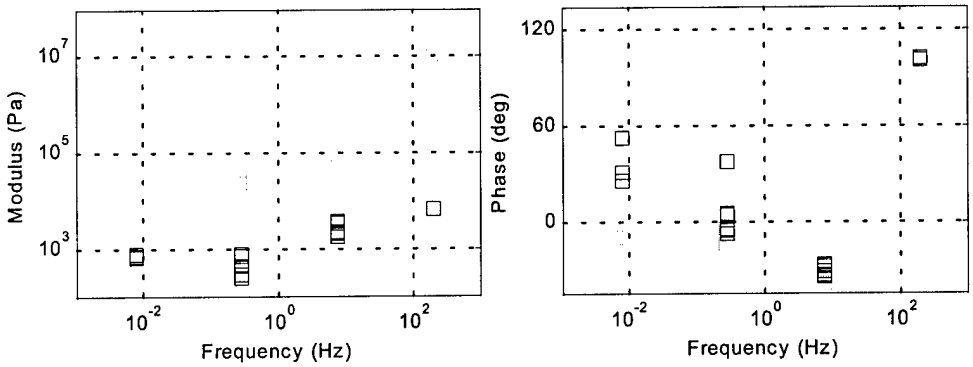

Figure 7: *in vitro* bovine liver results. ROSA-2 (grey), TeMPeST 1-D (black). Similar global behavior observed, but further analysis will be required to resolve discrepancies between instruments.

4.5 *Porcine liver test* in vivo

The *in vivo* testing shows similar results to the *in vitro* testing for ROSA-2, and also shows a much lower elasticity as measured by TeMPeST 1-D (Figure 8). Additional difficulties and noise in the data due to cardiac and pulmonary action make measurements less reliable.

Square wave testing *in vivo* demonstrated that the needle array can become clogged with continued use if it is not periodically rinsed to remove any deposits left behind by the fluids that "sweat" from the tissue itself. This was not observed in any testing with the adhesive disk.

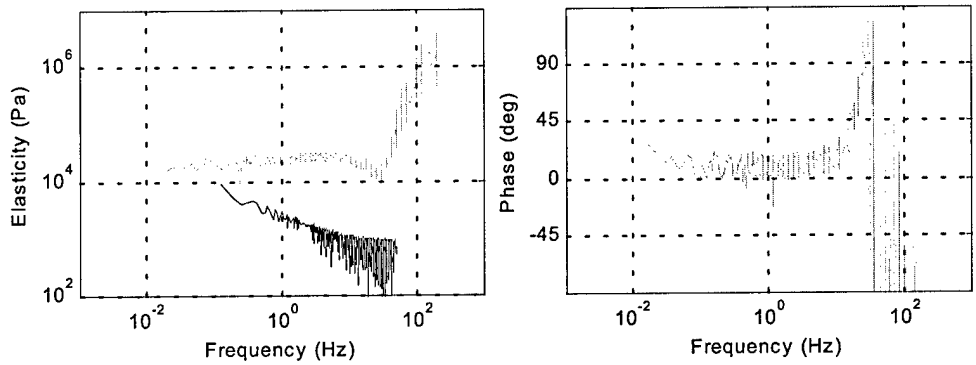

Figure 8: *in vivo* porcine liver results. ROSA-2 (grey) mean of 4 measurements; TeMPeST 1-D (black) n=12. Phase measurements for ROSA-2 unreliable above 50Hz; for TeMPeST 1-D corrupted by noise and omitted.

5. Conclusions and Future Work

This initial work in comparing rotary shear with indentation as soft tissue testing modes has shown agreement in the limited case of linearly elastic silicone gels, but more complex biological tissues result in widely differing elasticity measurements. Possible sources of the difference include the extremely simple tissue model employed, differing strain ranges and in the *in vivo* case, disturbances due to cardiac and pulmonary action.

The ROSA-2 evaluation indicates that non-slip contact can be maintained using either a needle array or adhesive disk, although use of the cyanoacrylate adhesive would not be suitable for survival animal tests, or human testing. An array of larger diameter needles might be less subject to the clogging problem and may be constructed in the future.

Future rotary shear instrumentation should include a torque sensor so that compliance can be measured at frequencies beyond the instrument-tissue system mechanical resonance. The next indentation probe should be insensitive to organ motion, and be able to measure absolute (not just relative) position. Finite element modeling based on real organ geometry will be pursued to better approximate the boundary conditions and finite deformations.

6. Acknowledgements

Support for this work has been provided by: a grant from the Deutsche Forschungs Gemeinschaft, project KA-1707/1-1, and a grant from the US Army, under contract number DAMD 17-01-1-0677. The ideas and opinions presented in this paper represent the views of the authors and do not, necessarily, represent the views of the Department of Defense.

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Measuring Parenchymal Properties of Perfused Solid Organs

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Harvard University, HST-MEMP 1997

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Quantifying the mechanical properties of soft tissues is crucial for understanding, validating, and advancing less invasive medical fields such as imaging, computer assisted medicine, and robotic surgery. Specifically, with the onset of minimally invasive surgery (MIS), surgeons are required to learn new skills for manipulating and visualizing 3D tissue from 2D images. Real time simulations of MIS are needed for training and planning purposes. The utility of these simulations lie in their realism: tissues need to look and behave appropriately. We are measuring the material properties of three major solid organ constituents, mathematically modeling the results, and combining these models to obtain a model of the whole organ that describes its behavior under surgically relevant conditions. The work presented here involves a new technique for measuring the material properties of parenchyma ex-vivo *under physiologic conditions.*

The complex nature of biological tissues makes characterizing their behavior a formidable challenge. Tissue testing devices must account for tissue inhomogeniety, anisotropy, geometric and mechanical nonlinearity under large deformations, incompressibility, loading rate dependency, and viscoelasticity. It has also been shown that although *ex vivo* tests are informative and easily controlled, biological tissues are drastically altered when removed from their natural (*in-vivo*) physiologic and boundary conditions.

A device has been developed to arbitrarily probe an internal, local volume of parenchyma under a nearly uniform stress distribution while approximating *in vivo* conditions. The device applies controlled displacements between a pair of embedded cylindrical bars ("T-needles") using a motor and linear potentiometer while measuring forces using a strain gauge-based force sensor. The device can test tissue under large strains (>30%) and low frequencies (<10 Hz) typical of surgical manipulations. Near physiologic conditions are obtained by placing the whole organ in a heated bath of Lactated Ringer's solution. A perfusion apparatus uses hydrostatic pressure generated by containers suspended at appropriate heights to maintain a constant, nonpulsatile flow throughout the liver.

Preliminary testing of both unperfused and perfused freshly excised whole porcine livers reveals a viscoelastic response with the unperfused organ being stiffer yet failing at a lower stress and strain than the perfused organ. The quasilinear viscoelastic model for force relaxation was fit using a sum of discrete time constants. The best fit was found for three time constants plus a steady state term. Although the values for single specimens are not definitive as of yet, they do serve to demonstrate the approaches ability to collect relevant parenchymal material property data under approximately *in vivo* conditions.

This work is part of a project in conjunction with the CIMIT Simulation group at Massachusetts General Hospital, funded by US Army Medical Research and Material Command.

A TECHNIQUE FOR MEASURING LOCAL INTERNAL MECHANICAL PROPERTIES OF PERFUSED SOLID ORGANS

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INTRODUCTION

Mechanical simulation of soft tissue is increasingly important for the development of new minimally invasive surgical applications. For surgical planning, the prediction of tissue deformation in response to instrument manipulation can improve accuracy of image-guided procedures. For surgical training, simulations permit new surgeons to safely practice a wide variety of procedures. To be effective in these applications, mechanical simulations must be realistic, so that the tissue behaves as in the living organism. This requires accurate *in vivo* constitutive models for tissues under the large deformations typical of surgical procedures.

The complexity of soft tissues makes characterizing their behavior a formidable challenge. Soft tissues exhibit viscoelastic properties, anisotropy, and inhomogeneity [1]. These tissues are drastically altered when no longer perfused, maintained at constant temperature, or bounded by the original surrounding structures as in the commonly tested *ex vivo* state [1, 2].

To make meaningful measurements requires an experimental environment that is close to the *in vivo* state and provides force and displacement measurements of the local tissue volume over time. *In vivo* devices have recently been developed that probe the tissue of interest from its surface and measure the corresponding force response [2-5]. However, these devices typically apply small perturbations to the organ surface and thus only measure superficial regions and do not account for large surgical strains. At present, imaging techniques (e.g. elastography) provide only qualitative or relative material property information for arbitrary organ geometry [6].

We have developed a new technique for probing the local mechanical properties of solid organs such as the liver, kidney, and spleen at arbitrary internal locations while approximating *in vivo* conditions. A pair of cylindrical bars is carefully inserted into the organ on each side of a local volume causing minimal damage to the volume of interest and allowing for a nearly uniform stress distribution. In the following sections we describe the apparatus and preliminary tests on porcine liver under physiologic conditions.

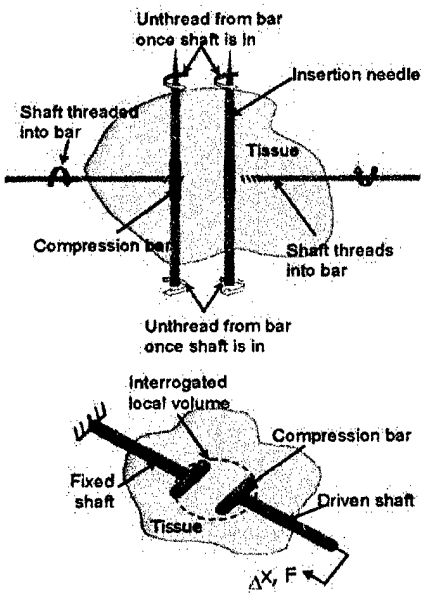

Figure1: (Top) Inserting the T-needles into the tissue. (Bottom) T-Needles probing local volume of interest.

METHODS

Experimental Apparatus

The device uses a pair of "T-needles" as mechanical probes for force-displacement measurements within an organ (Figure 1). To minimize damage to the tissue, the shafts and crossbars of the needles are inserted separately using a block alignment system, and assembled within the tissue. First, extensions are threaded onto the ends of the bars: the leading extension has a sharp point to cut through the tissue as it is inserted and the trailing extension provides the insertion force and controls the insertion direction. This needle assembly is inserted into the tissue and advanced to the correct position for mating with the

shaft. Second, the shafts are advanced into the tissue perpendicular to the insertion needles and threaded into the bars. The shafts are locked into place on their blocks and the bar extensions are removed. A cannula with a beveled end is inserted over the shaft on the driving side to minimize the effects of friction. The volume "resolution" of the device is defined by the diameter of the crossbars (3 mm in this prototype) and the spacing between the bars (19 mm).

The device applies controlled displacements between the two compression bars using a motor and linear potentiometer while measuring forces using a strain gauge-based force sensor. A computer controls the desired trajectory. The force and displacement data are recorded using a 16-bit analog-to-digital converter sampling at 5kHz. The device can test tissue under large strains (>30%) and low frequencies (<10 Hz) typical of surgical manipulations. Operation of the T-Needle prototype was confirmed using silicone tissue phantoms.

For the preliminary testing of porcine liver, the organ is placed on a floating plate in a bath of Lactated Ringer's solution, allowing free translation during testing to minimize static forces. To approximate *in vivo* conditions, a perfusion apparatus uses hydrostatic pressure generated by containers suspended at appropriate heights to maintain a constant, nonpulsatile flow throughout the liver. Flow is established to the hepatic artery at a pressure of approximately 120 mm Hg and to the portal vein at 50 mm Hg. The fluid is allowed to freely exit the liver at the hepatic vein into the basin where it is circulated by a pump to the suspended containers. An immersion heater maintains the temperature of the bath at 36 C.

Preliminary Protocol

Two preliminary tests using the T-needles were performed on both unperfused and perfused whole organs to determine the best protocol for future tests. Freshly harvested porcine livers were perfused with a mixture of normal saline and heparin and then iced for transport to the testing lab. The unperfused test used the liver from a 42.5 kg pig. Data was collected 3.5 hours after death. To test loading rate dependencies, the tissue was compressed at different ramp speeds, and then the force response was measured over time to determine the relaxation time constants. The ramp speeds ranged from 1 to 80 mm/s at a displacement of 2mm (11% strain) and then held for 60 sec. The perfused test used the liver from a 46 kg pig. Perfusion began 2.5 hours death, and testing began 20 minutes later. The ramp speeds ranged from 0.5 to 100 mm/s at a displacement of 7 mm (36% strain). Three data sets were collected at 2 and 6 hours post perfusion at a ramp speed of 1 mm/s. The last test for both organs compressed the tissue at a steady 1 mm/s rate until failure.

The data was filtered in MATLAB using a moving weighted average. Fung's quasilinear viscoelastic theory was chosen as the model to fit to the force relaxation data using a simplex method [1].

PRELIMINARY RESULTS

Results for both perfused and unperfused livers show a viscoelastic response with hysteresis, force relaxation, and nonlinear force-displacement. The unperfused organ was stiffer than the perfused organ, with a force of 1.2 N versus 0.6 N at 2 mm compression. The unperfused organ showed lower failure loading of 52% strain at 5 N versus 84% strain at 6.5 N for the perfused organ

Figure 2 shows the ramp and hold filtered data and model fit for the perfused organ at a ramp speed of 60 mm/s. The quasilinear model for force relaxation was fit using a sum of discrete time constants. The best fit was found for three time constants plus a steady state term. The fitted time constants for this data are 102 ms, 1.47 s, and 27.76 s with weights of 167, 140, and 225 mN respectively and a steady state value of 1.23 N. Lastly, between 2 and 6 hours into perfusion (4.5 hours post mortem) little or no change in the observed behavior was noted.

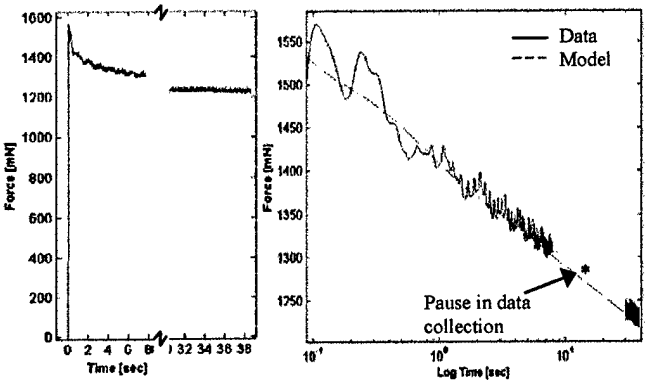

Figure 2: (Left) Ramp and hold of perfused organ at ramp speed = 60 mm/s. (Right) Hold phase with model fit

DISCUSSION

The preliminary results on porcine liver constitute a proof of concept test. Although the values for single specimens are not definitive, they do serve to demonstrate the approaches ability to collect relevant data under approximately *in vivo* conditions. These data are also collected from a relatively small region of the liver thus minimizing the volume over which inhomogeneities are averaged. The scale of the device can be reduced as needed to improve resolution by decreasing the bar diameter and the spacing between the two bars.

The force-displacement data illustrated by the preliminary tests can be directly used to evaluate aspects of the time response of the tissue. To determine the elastic response, however, requires more elaborate analysis. In particular, the variation of strain levels within the test volume (between and around the bars) makes it difficult to determine the nonlinear constitutive law from the data. One approach to this problem is the use of iterative finite element modeling. In this method, a constitutive law is assumed and a finite element simulation of the T-needle and tissue produces a prediction of the force-displacement relationship. Comparison with the experimental data is then used to update the constitutive parameters until a good fit is obtained. Issues of uniqueness of the parameters and adequacy of the experimental excitation must be addressed and validated against different loading conditions.

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Truth cube: Establishing physical standards for soft tissue simulation

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Abstract

Accurate real-time models of soft tissue behavior are key elements in medical simulation systems. The need for fast computation in these simulations, however, often requires simplifications that limit deformation accuracy. Validation of these simplified models remains a challenge. Currently, real-time modeling is at best validated against finite element models that have their own intrinsic limitations. This study develops a physical standard to validate real-time soft tissue deformation models. We took CT images of a cube of silicone rubber with a pattern of embedded Teflon spheres that underwent uniaxial compression and spherical indentation tests. The known material properties, geometry and controlled boundary conditions resulted in a complete set of volumetric displacement data. The results were compared to a finite element model analysis of identical situations. This work has served as a proof of concept for a robust physical standard for use in validating soft tissue models. A web site has been created to provide access to our database: http://biorobotics.harvard.edu/truthcube/ (soon to be http://www.truthcube.org).

Keywords: Physical standard; Real-time models; Model validation; Soft tissue mechanics; Surgical simulation

1. Introduction

Fast, realistic mechanical modeling of soft tissues remains a formidable challenge in the development of new medical applications. Simulations used in medical training, surgical planning, and image-guidance systems require real-time calculation of soft tissue deformation and interaction forces during manipulation of the simulated tissue. For soft tissue simulation to become a practical reality, further investigation of tissue biomechanical parameters, development of more efficient and accurate computer algorithms, and validation of simulated deformations against real in vivo data need to be addressed (Delingette, 1998).

Implementing modeling systems has proved difficult mainly due to the tradeoff between fast computation time and calculated deformation accuracy. Depending on the simulation's desired application, emphasis can be shifted towards the real-time aspect (e.g., surgical procedure training) or towards the accurate deformation aspect (e.g., material characterization) (Delingette, 1998). The nature of this tradeoff is not well understood, and it is difficult to evaluate the relative performance of new systems when speed, accuracy, tissue properties and geometry all vary. For instance, modeling tissue surfaces proves to be faster, but less accurate than modeling tissue volumes (Cotin et al., 1996). Similarly, spring-mass systems have limited accuracy but work well in real-time (Waters, 1992; Kuhnapfel et al., 1997; Downes et al., 1998), while finite element (FE) modeling has proved successful for accurately modeling small deformations of linearly elastic materials where calculation speed is not a paramount concern (Bro-Nielsen and Cotin, 1996; Cotin et al., 1996).

FE modeling serves as a possible soft tissue validation tool for simple geometries and completely defined materi-

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als and loading conditions. However, given that FE modeling is an approximation method in itself, the accuracy of its results heavily relies upon the quality of its input. Also, boundary conditions involving large deformations have difficulty converging when using FE modeling methods. Given these limitations, employing FE modeling to assess the accuracy of the various simplified algorithms used in real-time simulations of tissues with nonlinear material properties undergoing large deformations is of limited value.

It is the goal of this work to provide a method and preliminary data for quantifying the accuracy of soft tissue models. Towards this end we have developed a physical standard to assess the ability of an algorithm to precisely describe simulation of soft tissue under surgical manipulation. Ideally such a standard would take the form of stress, strain and displacement fields over the tissue surface and throughout the tissue volume for fully specified material properties, under a range of specified surgically relevant boundary conditions. The output of new modeling systems could then be compared to these standard physical results to validate and benchmark their performance (Fig. 1).

In this paper, we describe a practical physical standard for validation of soft tissue simulation. We used a 3D imaging technique to experimentally measure a well-characterized test phantom in the form of a cube of soft polymer. This 'truth cube' is made of a silicone rubber with fiducial spheres embedded in a 1 cm grid pattern throughout its $8\times8\times8$ cm^3 volume. We acquired computer tomography (CT) scans of the cube in undeformed and loaded states in both uniaxial compression and spherical indentation, and computed the relative displacement of each sphere using image processing techniques. These volumetric displacement results, along with details of the cube construction and boundary conditions in the two loading tests are reported. We also computed two FE models to compare to the experimental results. Lastly, we conclude with a discussion of plans for extension of this work (including applying this method to biological tissues), and an invitation for participation by others interested in the validation of fast large-deformation tissue modeling.

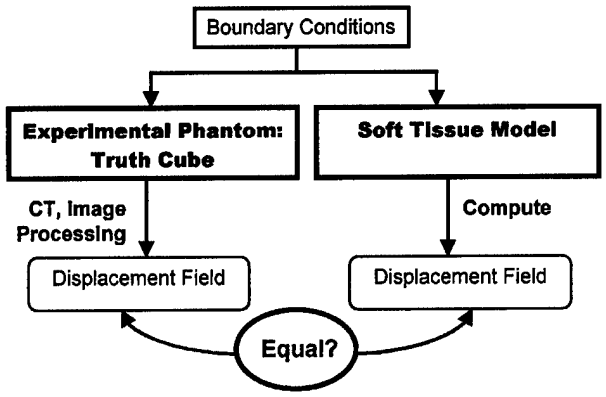

Fig. 1. Approach for validating soft tissue computational models. Boundary conditions (material property, geometric, loading conditions, etc.) are imposed on the experimental phantom and the model. The displacement fields in the phantom are measured using CT imaging and compared to the model's predicted results.

2. Methods

We have selected a cube as a simple, regular shape to assess the feasibility of the validation approach and to develop the required techniques. The considerations include materials for the tissue phantom and fiducials, 3-D imaging, image processing and data reporting.

2.1. Truth cube

We chose a two-part silicone rubber (RTV6166, General Electric) for the cube because its behavior is similar to soft tissues in the linear range (Wellman, 1999; Ottensmeyer, 2001): the material is soft but exhibits linear behavior to at least 30% strain. To enable tracking of the internal deformation of the cube we embedded small spheres as fiducials that would readily appear in CT scans but not significantly alter the material properties of the silicone. The choice of sphere material and size was motivated by the need for high contrast without creating imaging artifacts (Strumas et al., 1998): this implies a specific gravity well above silicone (0.98) but much less than steel (~8). To enable accurate segmentation and position estimation, the minimum diameter of the spheres had to be slightly larger than the distance between two successive scanning planes (1.0–1.25 mm) but small enough to avoid compromising the material properties of the silicone. Imaging tests using several commercially available spheres of different materials and sizes embedded in a sample of the silicone gel revealed that Teflon spheres (specific gravity 2.3) with a diameter of 1.58 mm fulfilled all of these criteria.

The mold for the cube had removable sides, with the bottom serving as a rigid permanent mounting plate that was roughened and dimpled to ensure complete adhesion of the silicone. The two-part silicone rubber was mixed in a 30:70 proportion to obtain material characteristics similar to that of mammalian liver (Ottensmeyer, 2001). A layer 1 cm deep was poured, the mold was placed in a vacuum chamber to remove air bubbles, and then allowed to set on a level surface before positioning spheres in a 7×7 matrix spaced 1 cm apart (Fig. 2). The spheres were laid on the silicone rubber using a matrix of positioning tubes and allowed to set into the rubber before the next layer was poured. The end result produced a silicone rubber cube 8 cm on each side with 7 rows and 7 columns of Teflon spheres in 7 layers, spaced 1 cm apart in each direction (Fig. 2).

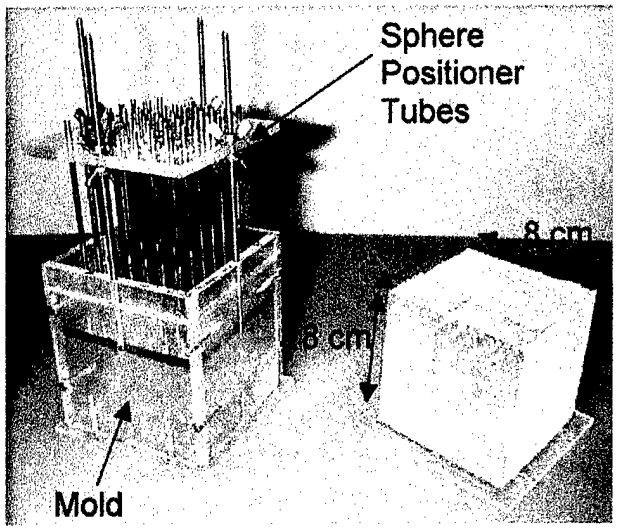

Fig. 2. Mold and internal sphere positioner (left) and resulting Truth Cube (right).

To ensure that the material properties of the silicone rubber were not affected by the addition of the 343 spheres, we performed indentation tests on three samples of the silicone rubber: alone, with sparse sphere density, and with 1 cm sphere spacing. Results indicated that the stiffness of the sample with the highest sphere density changed 2.0%, which is less than the 4.4% standard deviation of measurements of the plain sample. We thus conclude that the addition of the spheres had a negligible effect on the material properties of the silicone.

Both a small strain (<8%) uniaxial compression test and an indentation test were performed on a sample of the silicone rubber used to obtain material property characteristics. Results indicate a Young's modulus of 15.0±0.4 kPa. Poisson's ratio is near 0.5 for this polymer consistent with many polymers.

2.2. Experimental set-up

The silicone rubber phantom with embedded fiducial markers (Teflon spheres) was initially imaged under uniaxial compression to allow us to develop the technique and compare the results to a fully defined FE model. A subsequent test used a spherical indentation loading condition more typical of surgical manipulations.

The experimental set-up loaded the cube under controlled boundary conditions during the CT imaging process (Fig. 3). The fixture base for the uniaxial compression test was constructed of 2.54 cm thick rigid plastic and had cutouts that exactly fit the base of the truth cube to ensure consistent alignment within the set-up. Registration markers (1.27 cm diameter Delrin spheres) were attached to the fixture base to allow for uniform positioning of the experimental set-up on the CT table between tests performed at different times under the same loading conditions (i.e., when the whole apparatus had to be moved). However, since we scanned each loading condition once without needing to change the experimental set-up between successive scans, these markers were mainly used as a visual assessment feature and as an estimate of overall scanner accuracy.

The initial loading test, uniaxial compression, was accomplished with a 2.54 cm thick acrylic plate. This compression plate was attached to a vertical support by a low-friction pivot. The plate was loaded by weights applied to the end opposite the pivot (in addition to the weight of the plate itself). The design confined all metal

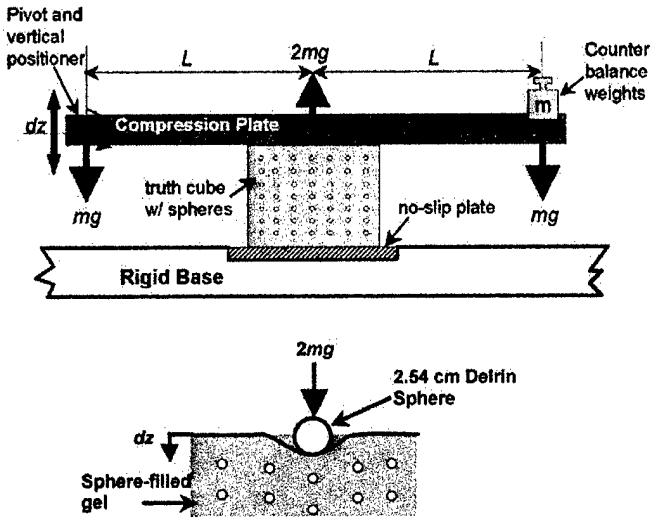

Fig. 3. Side view of the uniaxial compression experimental set-up (top) and close-up schematic of spherical indentation situation (bottom). L is the length from the loading points to the center of the cube, dz is the vertical motion, and m is the mass of the counter weights.

parts (the vertical support rods and weights) to the ends of the apparatus, so that they did not interfere with CT scanning of the cube in the middle of the apparatus. A linear dial indicator measured the distance the plate was translated (Fig. 4). A similar set-up was used for the large deformation spherical indentation test except that a 2.54 cm diameter Delrin spherical indentor mounted on a 1.9 cm diameter by 4.5 cm long Delrin cylinder was added to the compression plate (Fig. 4).

2.3. Experimental protocol

A first scan of the uniaxial compression experimental set-up was performed while the cube was unloaded to obtain a reference state of the internal sphere locations. The flat compression plate was then held level as it was lowered to a set displacement onto the oiled top surface of the cube. The oil was used to approximate a frictionless boundary condition. With the pivot end of the compression plate held in place, masses were added to a pocket in the other end until equilibrium was established as determined by level indicators. Three loading conditions were scanned: 4 mm, 10 mm, and 14.6 mm displacements, producing 5.0%, 12.5% and 18.25% nominal strain, respectively.

Once loaded, the cube was scanned in a General Electric LightSpeed CT scanner. Volumetric images of the truth cube were obtained using the following scanner settings: 120 kV, 180 mA, standard reconstruction type, and high quality scan mode. The field of view was 190 mm, producing a voxel size of $0.37\times0.37\times1.25$ mm^3. Each CT scan was composed of 99 slices, 1.25 mm thick (512×512 pixels, 16 bits), exported in DICOM format.

For the spherical indentation tests, the first scan was also conducted with the cube in an unloaded state for reference locations of the internal spheres. The compression plate with the indentor insert was then lowered in a manner similar to that of the uniaxial test. Two loading conditions were scanned: 18 mm and 24 mm displacements producing 22% and 30% local nominal strain, respectively. A third loading condition was attempted at 29 mm (36% nominal strain) but this caused the cube to fracture.

The indented cube was scanned in a similar manner and with the same settings as those used in the uniaxial compression test except that the field of view was 150 mm and a thinner slice thickness was used because a newer machine was made available that had better slice resolution (1.0 mm), producing a voxel size of $0.29\times0.29\times1.00$ mm^3. Each CT scan was composed of 133 slices, 1.0 mm thick (512×512 pixels, 16 bits) exported in DICOM format.

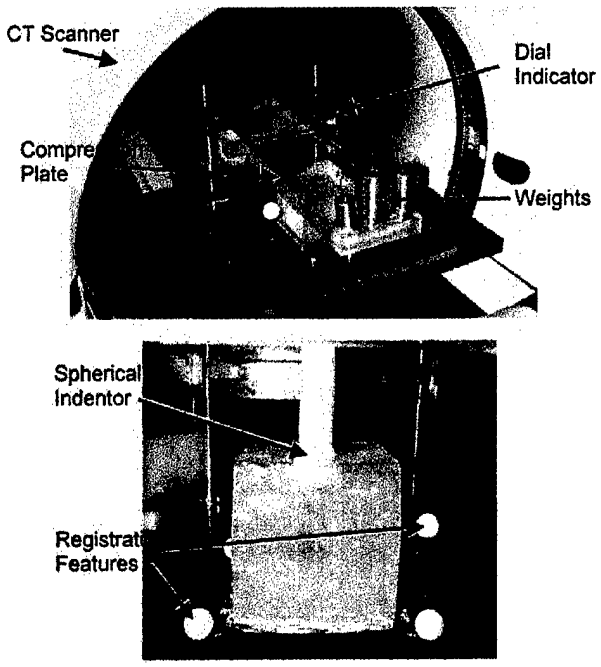

Fig. 4. Experimental test set-up for uniaxial compression (top) and spherical indentation (bottom).

2.4. Image processing

Commercial software (3D-Doctor, Able Software, Lexington, MA) was used for manipulating the volumetric images. The minor artifacts present in the lower part of the cube (due to the support plate in the uniaxial compression test) were filtered. Then the internal spheres in each of the scans were segmented from the silicone rubber with thresholding; this was relatively straightforward due to the good contrast between the spheres and the silicone rubber. After segmentation of the 343 internal spheres a surface model of each sphere was calculated and exported as a 3D polygonal model.

The 1.58 mm diameter spheres embedded in the silicone cube have the size of several voxels (the voxel size is 0.37 mm or 0.29 mm for uniaxial compression and spherical indentation, respectively), so the 3D segmentation process only provided an approximation of the shape and location of the spheres. To accurately determine the location of the center of each internal sphere, we implemented a least-squares algorithm that fit an analytic sphere to the set of points defined by the vertices of the polygonal model of each sphere. This algorithm is integrated in visualization software we developed to display polygonal models and vector fields of the relative displacement of the embedded spheres' centroids from their unloaded states to the various loaded states. We manually matched the relative displacement vectors of the spheres' centroids between the various loading conditions. Finally, the surface of the cube at each compression stage was extracted from the images. The large external registration spheres were also segmented in order to evaluate potential motion of the entire experimental set-up between successive scans.

2.5. Finite element model

A finite element model of the truth cube using commercial FE modeling software (ABAQUS v. 5.8, Hibbitt, Karlsson & Sorensen, Pawtucket, RI) was developed to compare with the experimental results. A simple coarse mesh was created for the uniaxial compression test to emulate models used in real-time soft tissue simulations. A more refined model was created to compare to the large deformation spherical indentation test results.

For the uniaxial test, a mesh of $1\times1\times1$ cm^3, 8-node, solid hexahedral linear elements was created so that the nodes of this model corresponded to the Teflon spheres. For the spherical indentation test, the truth cube was meshed with 1134 solid axisymmetric triangular elements to represent the cube as a cylinder with an 8 cm diameter (Fig. 8). Representing the cube as a cylinder was a good approximation as a comparison of the sphere displacement versus radial position for an orthogonal cut and a diagonal cut through the cube image data showed negligible difference in the sphere displacement versus radial position. The models' material properties were isotropic and linear with a Young's modulus of 15 kPa and an assumed Poisson's ratio of 0.499. For the uniaxial case, large deformation (i.e., nonlinear) analysis was employed using the boundary conditions (frictionless upper surface, fixed lower surface, and free side surfaces) and geometry extracted from the CT scans for the unloaded and 18.25% nominal strain cases. For the spherical indentation case, large deformation (i.e., nonlinear), axisymmetric analysis was employed using the boundary conditions (fixed contact between indentor and upper surface, free side surfaces, and fixed lower surface) and geometry extracted from the CT scans for the unloaded and 22% nominal strain cases.

3. Results

Figs. 5 and 6 illustrate the processing of the uniaxial compression test and spherical indentation test data, respectively. Fig. 5 begins with segmented CT data for a vertical slice through the center of the cube, in both unloaded (Fig. 5A) and 18.25% strain (Fig. 5B) cases. Fig. 5C represents the relative displacement field for the central vertical slice across all strains. Reconstructions of the surface of the cube for each strain state are shown in Fig. 5D.

Fig. 6 begins with a CT of the center slice of the unloaded state (Fig. 6A) followed by the 30% nominal strain case (Fig. 6B) and the vector field of the center slice displacements (Fig. 6C). Reconstructions of the surface for the 30% strain state are shown in Fig. 6D.

As an estimate of scanner accuracy, physical measurements of the spherical registration features were compared to measurements made on the raw CT scans. These measurements suggest that the accuracy of the scanner is less than 0.1 mm. Minimal errors were introduced by our segmentation procedure on the internal spheres (thresholding, polygonal modeling, sphere fitting, centroid calculating and tracking). Comparing the internal sphere location from raw to segmented data suggest that the error of the sphere locations is less than the size of one voxel in plane and less than half the size of the slice thickness out of plane. Therefore the estimated overall error in plane for the uniaxial compression and spherical indentation data are less than 0.37 mm and 0.29 mm, respectively, and less than 1.25 mm and 1.0 mm out of plane.

The predicted results from the center slice of the FE model of the simple uniaxial compression test are shown in Fig. 8A. There is a 3.5 mm maximum difference from the experimental results for a top surface displacement of 14.6 mm (18.25% nominal strain). The results predicted from a center slice of the more refined spherical indentation FE model at 22% nominal strain (18 mm displacement) are shown in Fig. 8B. Fig. 7 compares the internal sphere displacement results of the FE model to the measured data at 22% nominal strain for the spherical indentation case. The maximum difference between the model and the test results is 1.7 mm. This FE model was unable to converge at 30% nominal strain.

4. Discussion

This study demonstrates a technique for creating physical standards for validating the accuracy of real-time soft tissue simulation models. It was our goal to show that experimentally measured local internal displacement data from soft materials serves as a means of validating these models.

Our ideal physical standard would provide measurements of the deformation and stress fields over the surface and throughout the volume of soft tissues under large deformations (>30% strain) typical of surgical manipulation. This physical standard would also need to have well-characterized material properties similar to the simulated tissue, surgically relevant specified boundary conditions, and known geometry. Our truth cube has a modulus in the range of liver, E~15 kPa as reported by Ottensmeyer (2001). Imaging at strains of over 30% was easily accomplished. The external surface and the embedded fiducial spheres were readily segmented, which permitted calculation of the relative displacement fields throughout the volume. The result is a local displacement data set with well-characterized material properties and boundary conditions that can be used to assess the precision of soft tissue models under similar situations. Full displacement results and raw CT scans of both experiments are available on the project web site.

FE modeling is currently used to check the accuracy of soft tissue simulation models. We also compared our results to the output of these computational models. The

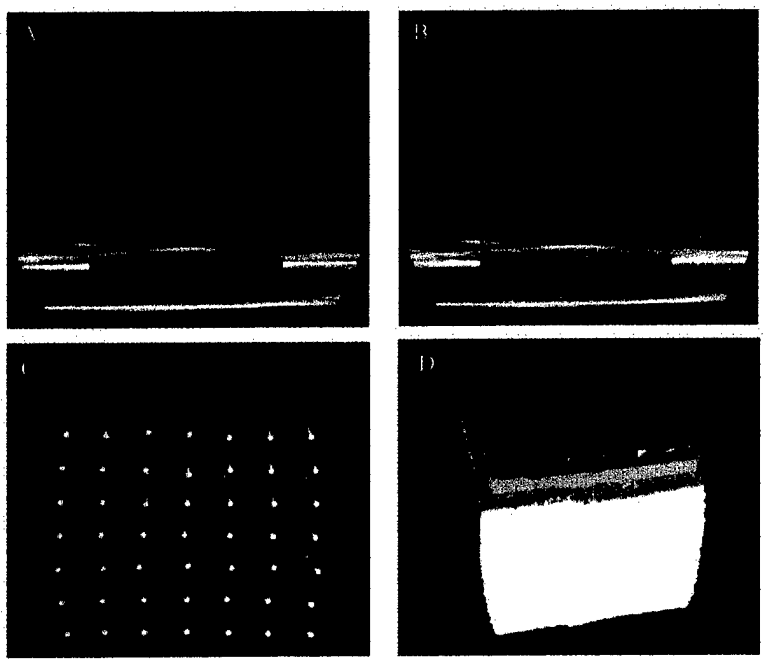

Fig. 5. The CT image of the central vertical plane of the Truth Cube after segmentation in both the unloaded (A) and maximally uniaxial compressed (B) states. Note the registration marker off to the side. Internal sphere trajectory and location in the central plane (C) (blue = unloaded, green = 5%, red = 12.5%, yellow = 18.25% strain). Outer surface of the cube in its four strain states (D).

simple FE model calculation presented for the uniaxial compression test used a minimal number of elements to reflect some of the speed versus accuracy tradeoffs of real-time tissue simulations. While the FE modeling and experimental data showed qualitative agreement, even with these simple loading conditions on a linearly elastic

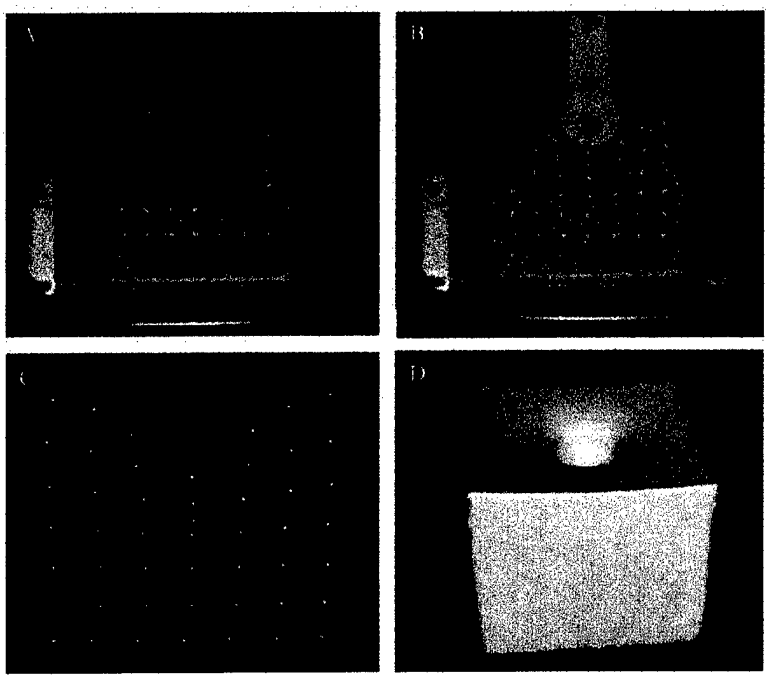

Fig. 6. CT of center vertical slice for spherical indentation in unloaded state (A) and under 30% nominal strain (B). Note the registration marker off to the side. The trajectory and locations of the internal spheres for the same slice is shown in (C) where blue represents no indentation, the 22% nominal strain case is shown in green, and the 30% nominal strain case in yellow. The surface for the 30% strain case is represented in (D).

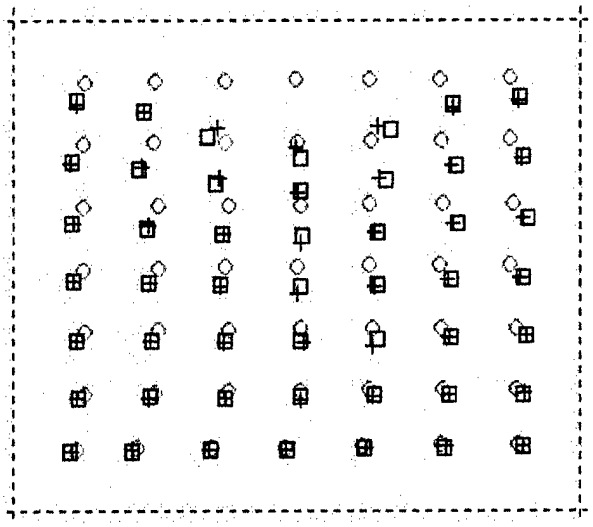

Fig. 7. Comparison of the measured internal sphere displacement (boxes) versus the FE model's predicted sphere displacement (crosses) for the 22% nominal strain spherical indentation case. The circles are the original internal sphere locations and the dashed line is the undeformed outer surface.

material the maximum single-point differences between the model and the experimental results were 3.5 mm for the 14.6 mm uniaxial displacement. Such an error may have significant consequences for applications such as surgical planning. Some portion of the difference may be due to inexact specification of the boundary conditions on the top of the cube during compression as well as the experimental error. Refinement of the model (e.g., smaller mesh size) should bring closer agreement to the experiment at the expense of increased computation time.

For the spherical indentation situation a finer resolution mesh was used to better replicate the experimental results. The maximum single-point differences between the model and the experimental results were relatively small (1.7 mm) for the 18 mm indentation case The model failed to converge for the 26.4 mm indentation situation (30% nominal strain) that was experimentally measured, and so no comparison could be drawn for this larger deformation. This demonstrates one of the limitations of using FE modeling as a validation tool: even the most robust FE models do to not readily converge for large deformations of the complex materials typically seen in surgical manipulations (Szekely et al., 2000).

Strains larger than 30% may be expected in surgical situations on biological tissues, i.e., organ retraction. Current FE modeling techniques for dealing with such gross deformation such as regridding are difficult to implement and of uncertain accuracy. This emphasizes the need for physical models as validation standards. We therefore conclude that although FE modeling is a powerful tool it may not be the most appropriate means of validating real-time soft tissue simulation models. The truth cube technique, however, results in an experimentally measured internal strain field with good resolution for all material properties, and thus should be the validation method of choice.

Several refinements to the measurement techniques are indicated by these results. First, we have only estimated the accuracy of the local internal sphere positions in this initial dataset. More precise accuracy specifications can be obtained through an analysis of the imaging and image processing procedures, and through reproducibility measurements. The raw scan data is available on the web site, so readers are welcome to develop improved image processing algorithms for this purpose. Another area for better characterization is the top surface boundary condition, where oiling the cube served to limit and regularize friction, but where a truly 'frictionless' condition did not apply. Fortunately, the contact area is readily measured during the experiment and in the processed CT images, so additional boundary information is available.

5. Future work

This initial study demonstrated the feasibility of experimental measurement of volumetric displacement fields for soft material phantoms under large strains, and provides some useful internal strain field data that can readily be used to validate soft tissue models. The truth cube has regular geometry and well-characterized material properties and loading conditions that was helpful for the development process, but fast tissue simulations must deal with conditions that are vastly different, involving very large deformations, irregular shapes and complex materials.

The next phase of this project is thus the measurement of biological tissue volumetric displacements, in the form of an entire organ. Preliminary plans call for measurement of a porcine liver immediately post mortem. We will determine the best ways to impose internal markers in the organ while minimizing damage to the tissue or affecting the material properties of the tissue, and to develop appropriate testing situations where the boundary conditions are completely identified. As an initial trial, 7 rows and 6 columns of the Teflon spherical fiducials were inserted in two layers about 2 cm deep via saline-filled blunt needles throughout a portion of the parenchyma of a freshly excised bovine liver. This liver was then imaged using the standard abdominal/pelvic settings for a human liver in an unloaded and a fully retracted state (strains >30%). This state is similar to how a surgeon would bend the liver out of the way to gain access to abdominal structures below. The results shown in Fig. 9 (the experimental set-up followed by CT slices of the unloaded and retracted liver) suggest that only minor modifications

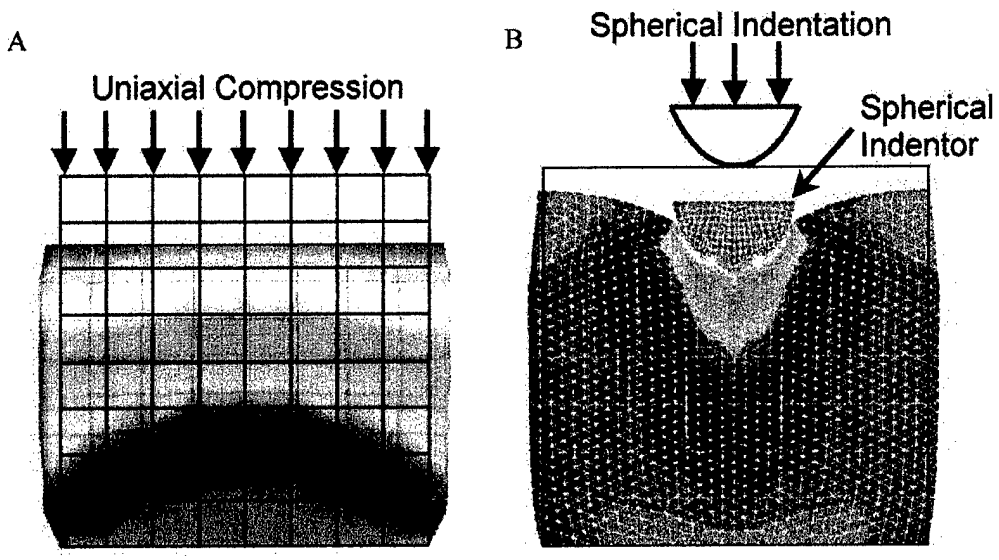

Fig. 8. Center slice of the uniaxial compression coarse mesh under 18.25% strain (A). Center slice of the refined spherical indentation FEM mesh displaying the results of the 22% strain experiment (B). The magnitude of the strain is coded as color with red indicating the highest strain and violet indicating the lowest. Note that the undeformed model is outlined in black.

to our current technique will be needed to obtain volumetric data of real soft tissue.

While these biological material tests have obvious advantages, the material properties will not be well-characterized as in the phantom tests. The identification of these material properties is an active area of research, and the data sets may be useful for solving the inverse problem of estimating these material properties from the displace-

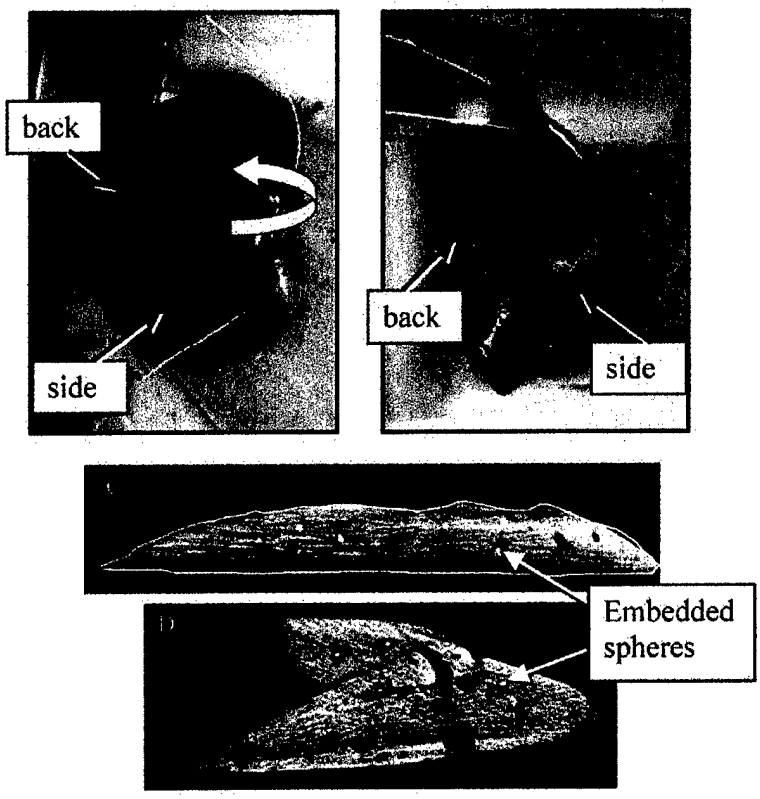

Fig. 9. Bovine liver retraction experimental set-up and results. The liver was cut to size, embedded with Teflon spheres, and imaged in the unloaded (A) and retracted (B) states. CT slices of the undeformed (C) and of the retracted liver (D). Spheres and surfaces are highlighted.

ment data. In any case, the displacement data alone will provide a source of information for the development and validation of fast simulation systems.

As we proceed, we welcome comments and suggestions on all aspects of the project, from tissue selection and loading conditions to experimental methods and data analysis. Further information is provided on the web site at: http://biorobotics.harvard.edu/truthcube (soon to be www.truthcube.org). Contributions of a broad cross-section in the tissue modeling community will help ensure the development of a robust physical standard for the benchmarking of real-time soft tissue simulations.

Acknowledgements

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References

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Cotin, S., Delingette, H., Clement, J.M., Bro-Nielsen, M., Ayache, N., Marescaux, J., 1996. Geometrical and physical representations for a simulator of hepatic surgery. In: MMVR '96. IOS Press, Amsterdam, The Netherlands, pp. 139–150.

Delingette, H., 1998. Towards realistic soft tissue modeling in medical simulation. IEEE: Special Issue in on Virtual and Augmented Reality in Medicine 86, 1–12.

Downes, M., Cavusoglu, M., Gantert, W., Way, L., Tendick, F., 1998. Virtual environments for training critical skills in laproscopic surgery. In: MMVR '98. IOS Press, Amsterdam, The Netherlands, pp. 316–322.

Kuhnapfel, U.G., Kuhn, C., Hubner, M., Krumm, H.G., MaaE, H., Neisius, B., 1997. The karlsruhe endoscopic surgery trainer as an example for virtual reality in medical education. Minim. Invasive Ther. Allied Technol. 6, 122–125.

Ottensmeyer, M.P., 2001. Minimally invasive instrument for in vivo measurement of solid organ mechanical impedance. PhD Thesis, Department of Mechanical Engineering, Massachusetts Institute of Technology Cambridge, MA.

Strumas, N., Antonyshyn, O., Yaffe, M.J., Mawdsley, G., Cooper, P., 1998. Computed tomography artifacts: an experimental investigation of causative factors. Can. J. Plast. Surg. 6 (1), 23–29.

Szekely, G., Brechbuhler, C., Dual, J. et al., 2000. Virtual reality-based simulation of endoscopic surgery. Presence 9 (3), 310–333.

Waters, K., 1992. A physical model of facial tissue and muscle articulation derived from computer tomography data. Visualization in Biomedical Computing. Chapel Hill, NC. In: SPIE Proc. VBC'92.

Wellman, P.S., 1999. Tactile imaging. PhD Thesis, Division of Engineering and Applied Sciences, Harvard University Cambridge.

Appendix B: selected CVs and BioSketches

Dawson, Steven L., M.D.

Howe, Robert D., Ph.D.

Ottensmeyer, Mark P., Ph.D.

Kerdok, Amy E., M.S

Galea, Anna M, Ph.D.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE
Steven L. Dawson, MD	Program Lead, Medical Simulation, CIMIT

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE (*if applicable*)	YEAR(s)	FIELD OF STUDY
State University of New York at Buffalo	BA	1974	Biology
Tufts University	MD	1978	Medicine
Medical-Surgical Intern, Newton-Wellesley Hospital		1978-1979	
Radiology Residency, Massachusetts General Hospital		1979-1982	
Imaging and Interventional Radiology Fellowship, Massachusetts General Hospital		1982-1984	

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

Professional Experience:

1982-1986	Radiologist, Waltham Hospital
1986-1990	Radiologist, Lahey Clinic
1990-Present	Interventional Radiologist, Massachusetts General Hospital
1997-1999	Director, New Initiatives, Center for Innovative Minimally Invasive Therapy
1998-1999	Director, Education, Center for Innovative Minimally Invasive Therapy
1998-Present	Program Lead, Medical Simulation, CIMIT
1994-2001	Assistant Professor, Harvard Medical School
2001-	Associate Professor, Harvard Medical School

Honors:

1974 Phi Beta Kappa

1992 RSNA Exhibit: Lee MJ, Dawson SL, Mueller PR. Percutaneous management of periportal biliary malignancies with metallic endoprostheses: results, technical problems and causes of failure. Certificate of Merit Award.

1990 Associate Editor, *Seminars in InterventionalRadiology*

1991 Reviewer, *American Journal of Roentgenology*

1994 Member, American College of Radiology Expert Panel on Interventional Radiology of ACR Task Force on Appropriateness Criteria

1994 Fellow, Society of Cardiovascular and Interventional Radiology

1996 Technology Reviewer, Image Guided Medicine, Technology Applications Review, National Technology Transfer Center

1997 Examiner, American Board of Radiology Subspecialty Examination in Vascular and Interventional Radiology

1995 Corresponding Fellow, Cardiovascular and Interventional Radiology Society of Europe

1996 External Reviewer, Biomedical Programs, Battelle/Pacific Northwest National Labs

1999 Session Chair and Lecturer, US Public Health Service and National Cancer Institute Joint Working Group on Image Guided Diagnosis and Treatment

2000 Partners Excellence Award

Research Interests:

Minimally invasive treatments of visceral cancer using image guidance, computer-based simulations for medical learning

Selected Publications:

Lee MJ, Mueller PR, Dawson SL, Gazelle GS, Hahn PF, Goldberg MA, Boland GW. Percutaneous Ethanol Injection for the Treatment of Hepatic Tumors: Indications, Mechanism of Action, Technique and Efficacy. AJR 1995; 164: 215-220.

Goldberg SN, Gazelle GS, Dawson SL, Rittman WJ, Mueller PR, RosenthalDI. Tissue Ablation with Radiofrequency Using Multiprobe Arrays. Academic Radiology 1995; 2: 670-674.

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Rattner DW, Dawson SL. The Operating Room of the Future, in Current Review of Laparoscopy, Churchill Livingston, 1995, 185-193s.

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Goldberg SN, Ryan TP, Hahn PF, Schima W, Dawson SL, Lawes KR, Mueller PR, Gazelle GS. Transluminal radiofrequency tissue ablation with use of metallic stents. JVIR 1997; 8: 835-843.

Dawson SL, Kaufman JA. The Imperative for Medical Simulation. Proceedings of the IEEE 1998; 86 (3): 479-483.

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Shaffer D, Meglan D, Ferrell M, and Dawson S. Virtual Rounds: simulation-based education in procedural medicine. In: Pien H, editor. Battlefield Biomedical Technologies, Proc. SPIE 1999; 3712:99-108 .

Shaffer DW, Dawson SL, Meglan D, Ferrell M. Simulation Based Education in Procedural Medicine, Proc. SPIE Conference on Battlefield Biomedical Technologies, v.3712, April, 1999.

Bauer JJ, Magee JH, Moses G, Leitch R, Dawson SL . Medical simulation training initiative (MSTI), SPIE Conference on Battlefield Biomedical Technologies, v.4037, April, 2000.

Cotin SC, Dawson SL. CAML: a general framework for the development of medical simulation systems. SPIE Conference on Battlefield Biomedical Technologies, v.4037, April, 2000.

Dawson SL, Cotin S, Meglan D, Shaffer DW, Ferrell MA. Desigining a computer-based simulator for interventional cardiology training [with editorial]. Catheterization and Cardiovascular Interventions, 2000: 51; 522-528.

Shaffer, DW, Dawson, SL, Meglan, D, Cotin, S, Ferrell, M, Norbash, A, Muller, J. (2000) "Design Principles for the use of simulation as an aid in interventional cardiology training." Minimally Invasive Therapy and Applied Technologies, 10:2.

NAME	POSITION TITLE
Robert D. Howe, Ph.D.	Gordon McKay Professor of Engineering

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)

INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
Reed College – Portland, OR	B.A.	1979	Physics
Stanford University – Stanford, CA	M.S.	1985	Mechanical Engineering
Stanford University – Stanford, CA	Ph.D.	1990	Mechanical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds two pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Employment

1979-1981 Electronics Engineer, Kratos Display Systems. Los Gatos, CA.
1981-1983 Research Physicist, High Temperature Gasdynamics Laboratory, Stanford University
1984-1990 Research Assistant, Mechanical Engineering Dept. Stanford.
1990-1994 Assistant Professor of Mechanical Engineering, Harvard University.
1994-1997 Associate Professor of Mechanical Engineering, Harvard University.
1997-present Gordon McKay Professor of Engineering, Division of Engineering & Applied Sciences, Harvard Univ.

Selected Honors and Professional Service

National Science Foundation Young Investigator Award, 1993.

Best poster award, Sixth International Meeting of the Society for Minimally Invasive Therapy, Berlin (with William Peine), 1994.

Associate editor, IEEE Transactions on Robotics and Automation, 1994-1998.

Funding Review Panel Member, National Science Foundation, 1994, 2000.

Whitaker Foundation Biomedical Engineering Research Grant (Career Development Award), 1995.

Chair and Organizer, Annual Symposium on Haptic Interfaces for Virtual Environment and Teleoperator Systems, ASME International Mechanical Engineering Congress and Exposition, 1996-1998 (with Susan J. Lederman).

Program Committee, International Symposium on Medical Robotics and Computer Assisted Surgery/MICCAI, 1994, 1995, 1997, 1998, 2000.

Program Committee, Frontiers of Engineering Symposium, National Academy of Engineering, Irvine, CA, Nov. 1998.

Selected Publications

Wellman, P.S, Dalton, E.P., Krag, D., Kern, K.A., Howe, R.D. "Tactile Imaging of Breast Masses: First Clinical Report," Archives of Surgery, in press.

A. Z. Hajian and R. D. Howe, "Biomechanics of Manipulation: Grasping the Task at Hand," in J. Winters and P. Crago,

eds, Neural Control of Posture and Movement, Springer-Verlag, 2000, pp.382-389.

F. Lai and R.D. Howe, "Evaluating Control Modes for Constrained Robotic Surgery," Proc. IEEE International Conference on Robotics & Automation, San Francisco, April 2000, pp. 603-609.

Pawluk, D.T.V. and Howe, R.D. "Dynamic contact of the human fingerpad against a flat surface." ASME Journal of BiomechanicalEngineering 121(6):605-611, December 1999.

M. Shibata and R.D. Howe, "Effect of Gloving on Perceptual and Manipulation Task Performance,"in N. Olgac, ed., Proc. ASME Dynamic Systems and Control Division, 1999, DSC-Vol. 67.

P. Dupont, T. Schulteis, P. Millman, and R. D. Howe, "Automatic Identification of Environment Haptic Properties," Presence 8(4):392-409, August 1999.

Pawluk, D.T.V. and Howe, R.D. "Dynamic Lumped Element Response of the Human Fingerpad." ASME Journal of BiomechanicalEngineering 121(2):178- 184, April 1999.

R. D. Howe and Y. Matsuoka, "Robotics for surgery," Annual Review of Biomedical Engineering, 1:211-240, 1999.

W.J. Peine and R.D. Howe, "Do humans sense finger deformation or distributed pressure to detect lumps in soft tissue?," in R.J. Furness, ed., Proc. of the ASME Dynamic Systems and Control Division, ASME International Mechanical Engineering Congress and Exposition, Anaheim, Nov. 19-20, 1998, DSC-Vol. 64, pp. 273-278.

D. T. V. Pawluk, J. S. Son, P. S. Wellman, W. J. Peine, and R. D. Howe. "A Distributed Pressure Sensor for Biomechanical Measurements," ASME Journal of Biomechanical Engineering 102(2):302- 305, April 1998.

A. Z. Hajian and R. D. Howe, "Identification of the mechanical impedance at the human finger tip," ASME Journal of Biomechanical Engineering, 119(1):109-114, Feb. 1997. Also presented at the International Mechanical Engineering Congress, American Society of Mechanical Engineers, Chicago, IL, November 1994, Proceedings ed. C. J. Radcliffe, DSC-vol. 55-1, p. 319-327.

Pawluk D. and Howe, R.. A Holistic Model of Human Touch. In J.M. Bower (Ed.) Computational Neuroscience Trends in Research, Plenum Press, New York, pp. 759-764, 1997.

P. E. Dupont, T. M. Schulteis, and R. D. Howe , "Experimental Identification of Kinematic Constraints, Proc. IEEE International Conference on Robotics and Automation, Albuquerque, New Mexico, April 20 - 25, 1997, pp. 2677-82.

R. D. Howe, D. A. Kontarinis, W.J. Peine, and P. W. Wellman, "Tactile displays for increased spatial and temporal bandwidth in haptic feedback," in Y. Shirai and S. Hirose, eds., Robotics Research: The Eighth International Symposium, October 4-7, 1997, Hayama, Japan, Springer-Verlag, 1998.

P. S. Wellman, R. D, Howe, N. Dewagan, M. A. Cundari, E. Dalton, K. A. Kern, "Tactile Imaging: A Method for Documenting Breast Masses," Proc. 1st Joint BMES/EMBS Conference, Atlanta, Oct. 13-16, 1999, p. 1131.

D.T.V. Pawluk, R.D. Howe, "Dynamic Contact Mechanics of the Human Fingerpad with a Flat Surface," Biomedical Engineering Society Annual Meeting, Cleveland, October 11 , 1998.

D. T. V. Pawluk and R. D. Howe, "Contact pressure distribution on the human finger pad," 26th Congress of the International Society of Biomechanics, Tokyo, August 25-29, 1997, p. 335.

Pawluk, D.T.V., Peine, W.J., Wellman, P.S. and Howe, R.D., "Simulating Soft Tissue with a Tactile Shape Display," Advances in Bioengineering, ASME BED-Vol. 36, pp. 253-4.

P. S. Wellman and R. D. Howe, "Modeling probe and tissue interaction for tumor feature extraction," 1997 ASME Summer Bioengineering Conference, Sun River, Oregon, June 1997, BED-Vol. 35, p. 237-8.

D. T. V. Pawluk and R. D. Howe, "Mechanical impedance and energy dissipation in the human finger pad," 1997 ASME Summer Bioengineering Conference, Sun River, Oregon, June 1997, BED-Vol. 35, p. 591-592.

W.J. Peine and R. D. Howe, "Finger pad shape in lump detection," 1997 ASME Summer Bioengineering Conference, Sun River, Oregon, June 1997, BED-Vol. 35, p. 593-594.

R. D. Howe, W. J. Peine, D. A. Kontarinis, and J. S. Son, "Remote palpation technology," IEEE Engineering in Medicine and Biology, 14(3):318-323, May/June 1995.

NAME	POSITION TITLE
Mark P. Ottensmeyer, Ph.D.	Research Fellow, Simulation Group, CIMIT, MGH

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)

INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
McMaster University, Hamilton, Ontario, Canada	B.Eng.Mgt	1994	Mechanical Engineering and Management
Massachusetts Institute of Technology, Cambridge, MA, USA	M.S.M.E.	1996	Mechanical Engineering
	Ph.D.	2001	Mechanical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds two pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Research Experience

1991-1993 (summers) Research Assistant, McMaster University, Canada. Performed wind-tunnel experiments on electrical transmission line models to study transmission line galloping phenomenon. PI: Prof. Ozden F. Turan.

1993-1994 (summers) Research Assistant, Flexible Manufacturing Systems Laboratory, McMaster University, Canada. Developed power-up calibration system for AdeptOne industrial robot. PI: Prof. Hoda ElMaraghy.

1994-1996 Research Assistant, Human-Machine Systems Laboratory, M.I.T. Conducted research into and designed experiments on human performance in teleoperated surgery exercises with system time delays. PI: Prof. Thomas B. Sheridan.

1996-1998 Research Assistant, Haptics Group, Artificial Intelligence Laboratory, M.I.T. Developed thermal feedback device for virtual environment touch interface. PI: Dr. J. Kenneth Salisbury

1998-2001 Research Assistant, Haptics Group, Artificial Intelligence Laboratory, M.I.T. Developing minimally invasive surgical instruments for measuring mechanical properties of living organ tissues, performing in vitro and *in vivo* measurements. PI: Dr. J. Kenneth Salisbury

2001-present Research Fellow, Simulation Group, Center for Integration of Medicine and Innovative Technology, Massachusetts General Hospital. Developing minimally invasive surgical instruments for measuring mechanical properties of living organ tissues, performing in vitro and *in vivo* measurements, designing simulator for surgical training. P.I. Dr. Steven Dawson

Honors

1989	Ontario Scholarship
	Sir Isaac Newton Physics Contest, Book award
1990	S.L. Squire Scholarship, McMaster University
	Harry Lyman Hooker Scholarship, McMaster University
1991	Whidden Hall Residence Scholarship, McMaster University
	Harry Lyman Hooker Scholarship, McMaster University

1992	Shell Canada Series Scholarship, McMaster University
	Ray Lawson Scholarship, McMaster University
1993	Shell Canada Series Scholarship in Engineering and Management, McMaster University
	Ray Lawson Scholarship, McMaster University
1996-1998	Post Graduate Scholarship, National Sciences and Engineering Research Council, Canada

Society Memberships
Sigma Xi, The Scientific Research Society, Full Student Member, 5 years
ASME, Associate Member, 4 years

Publications

Refereed journal papers:

Ottensmeyer, Mark P., Hu, Jianjuen, Thompson, James M., Ren, Jie, Sheridan, Thomas B.: Investigations into performance of minimally invasive telesurgery with feedback time delays, *Presence: Teleoperators and Virtual Environments*, vol. 9, no.4, 369-82, 2000.

Ottensmeyer, Mark P.: TeMPeST 1-D: an instrument for measuring solid organ soft tissue properties, *Experimental Techniques*, vol. 26, no. 3, 28-50, May/June 2002.

Kerdok, A.E., Cotin, S.M., Ottensmeyer, M.P., Galea, A.M, Howe, R.D., Dawson, S.L.: Truth Cube: Establishing Physical Standards for Real Time Soft Tissue Simulation, *Medical Image Analysis*, vol. 7, pp283-291, 2003.

Conference papers:

Thompson, J.M., Ottensmeyer, M.P., Sheridan, T.B.: Human Factors in Tele-inspection and Tele-surgery: Cooperative Manipulation under Asynchronous Video and Control Feedback. Proceedings of the Medical Image Computing and Computer-Assisted Intervention 1st International Conference, MICCAI '98, Cambridge, MA. pp368-377. 11-13 Oct 1998.

Ottensmeyer, Mark P., Ben-Ur, Ela, Salisbury, Dr. J. Kenneth.: Input and Output for Surgical Simulation: Devices to Measure Tissue Properties *in vivo* and a Haptic Interface for Laparoscopy Simulators. Proceedings of Medicine Meets Virtual Reality 2000, Newport Beach, CA. IOS Press. pp236-242. 27-30 Jan 2000.

Ottensmeyer, M.P., Salisbury, J.K.: *In vivo* mechanical tissue property measurement for improved simulations. Proceedings of Digitization of the Battlespace V and Battlefield Biomedical Technologies II, R. Suresh and H.H. Pien, Eds., Proc. SPIE 4037, Orlando, FL. pp286-293. 24-28 Apr 2000.

Bruyns, Cynthia, Ottensmeyer, Mark.: Measurements of Soft-Tissue Mechanical Properties to Support Development of a Physically Based Virtual Animal Model. MICCAI 2002. Proceedings of the Medical Image Computing and Computer-Assisted Intervention 5th International Conference, Tokyo, Japan, pp35-43. 25-28 Sept 2002.

Cotin, Stephane, Stylopoulos, Nicholas, Ottensmeyer, Mark, Neumann, Paul, Rattner, David, Dawson, Steven. Metrics for Laparoscopic Skills Trainers: The Weakest Link!. *MICCAI 2002. Proceedings of the Medical Image Computing and Computer-Assisted Intervention 5th International Conference,* Tokyo, Japan, accepted for publication. 25-28 Sept 2002.

Other publications:

Ottensmeyer, Mark Peter. Telerobotic Surgery: Feedback Time Delay Effects on Task Assignment. Master's Thesis in Mechanical Engineering at the Massachusetts Institute of Technology. © M.I.T., 1996.

Ottensmeyer, Mark Peter. Minimally Invasive Instrument for In Vivo Measurement of Solid Organ Mechanical Impedance. Doctoral Thesis in Mechanical Engineering at the Massachusetts Institute of Technology, © M.I.T., 2001.

Amy Elizabeth Kerdok

6 Craigie Circle Suite 41
Cambridge, MA 02138
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Education

HARVARD UNIVERSITY — Cambridge, MA, Expected 2004

- Candidate for Ph.D. in Engineering Sciences, Division of Engineering and Applied Sciences
- Enrolled in HST program for Medical Engineering/Medical Physics which includes Approx. 1 year of medical and clinical coursework

MASSACHUSETTS INSTITUTE OF TECHNOLOGY — Cambridge, MA, September 1999

- MS, Mechanical Engineering
- GPA: 4.8 / 5.0

RENSSELAER POLYTECHNIC INSTITUTE — Troy, NY, May 1997

- BS, Biomedical Engineering; Concentration: Mechanical engineering
- Minor: Management
- GPA: 3.97 / 4.0 (*summa cum laude*)

Research Experience

HARVARD UNIVERSITY — Cambridge, MA, 2000-present

Research Assistant

- Area: Soft Tissue Biomechanics
- Advisor: Prof. Robert Howe, Harvard University Biorobotics Laboratory
- Responsibilities: Mechanical design of soft tissue material property testing device, finite modeling of soft tissue behavior, clinical data collection

MASSACHUSETTS INSTITUTE OF TECHNOLOGY — Cambridge, MA, 1998-2000

Research Assistant

- Area: Sports Biomechanics
- Advisors: Prof. Thomas A. McMahon, Harvard University, and Dr. Hugh M. Herr, MIT Leg Laboratory
- Responsibilities: Experimental apparatus design, human experimentation, modeling of the dynamic parameters of running

HARVARD MEDICAL SCHOOL, New England Regional Primate Center — Southboro, MA, Summer 1994

Intern, dept. of Cardiovascular Medicine with Dr. Stephen Vatner

- Assisted as the third person in open heart animal surgeries
- Assisted Dr. Luc Hittenger in experiment on Left Ventricular Hypertrophy Dogs

Teaching Experience

HARVARD UNIVERSITY — Cambridge, MA, 2002, 2003

Teaching Fellow

- Assisted in teaching ES51 "Computer-Aided Machine Design"
- Developed the curriculum for and ran the laboratories to teach undergraduate students engineering design via SolidWorks and computer-aided milling machines

Teaching Fellow — Spring 2001
- Assisted in teaching ES149 "Muscles, Reflexes, and Locomotion"
- Conducted weekly review sections, graded problem sets

Relevant Design Coursework

MASSACHUSETTS INSTITUTE OF TECHNOLOGY — Cambridge, MA, Spring 1998
- Product Design and Development team project
- Designed and manufactured prototype of an energy returning forearm crutch

RENSSELAER POLYTECHNIC INSTITUTE — Troy, NY, 1997
- Senior Design Project in Biomedical Engineering
- "Improving the Safety of Snowboarding": designed a new rotating front binding, designed a new heel retention mechanism for the boot, developed manufacturing and testing standards, and performed biomechanical testing of the knee joint

RENSSELAER POLYTECHNIC INSTITUTE — Troy, NY, Fall 1994
- Introduction to Engineering Design team; team leader
- Delegated duties to design a pipe inspection robot to plot grade vs. distance

Industrial Experience

MEDSOURCE INC (FORMALLY ACT MEDICAL INC.) — Newton, MA, 2000
Project Engineer (graduate student intern)
- Project manager for 1 project, co-managed 2 other projects
- Responsibilities: proposal writing, customer relations, design and development of various medical products (concept, prototyping, testing, quality, manufacturing), consultation

STRYKER (formally HOWMEDICA INC.) — Rutherford, NJ, Summer 1995
Research Technician, R&D, Performance Engineering
- Operated MTS 810 and 407 controller single axis dynamic testing machines
- Designed orthopedic testing fixtures and molds (under ISO, ASTM, and FDA standards)

Leadership Experience

HARVARD UNIVERSITY — Cambridge, MA, 2002-present
- Harvard College Science Mentoring Program for women: graduate women in science are matched up with sophomore women

- Harvard/MIT Health Sciences and Technology Medical Engineering/Medical Physics Admissions committee — 2001-present

MASSACHUSETTS INSTITUTE OF TECHNOLOGY — Cambridge, MA, 2002-present
- Biomatrix Mentoring Program: Graduate students and members of industry and academia are matched up with each other as well as with undergraduate biomedical engineering students

RENSSELAER POLYTECHNIC INSTITUTE — Troy, NY, 1996
- Student Representative for the Archer Center for Student Leadership: Organized Anderson Consulting Leadership conference — Spring 1996
- Engineering Leadership course — 1995-1996
- Professional Leadership Program, selected group of juniors: Developed skills for team and leadership aspects of the professional world

- Pi Beta Phi executive board elected positions: Housing Committee Representative, Membership Chairman — 1995-1996

Selected Awards & Honors

- Faculty Achievement Award, Rensselaer Polytechnic Institute — 2003
- Harvard University Certificate of Distinction in Teaching — 2001
- Whitaker Fellowship, for advanced studies in Biomedical Engineering — 1997-2003
- Sigma Xi (national research honor society) — Inducted 1998
- Livingston W. Houston Citizenship Award, Rensselaer Polytechnic Institute — 1997
- Paul B. Diach Award, top biomedical student, Rensselaer Polytechnic Institute — 1997
- Tau Beta Pi (national engineering honor society) — Inducted 1996
- Founder's Award for Excellence, Rensselaer Polytechnic Institute — 1995
- Rensselaer Alumni Scholarship — 1993
- Rensselaer Polytechnic Institute medal (mathematics and science scholarship) — 1992

Athletics

HARVARD UNIVERSITY — Cambridge, MA

- Harvard University Cycling Association: women's category A road racing, team Captain — 2001-present

Boston-to-New York AIDS Ride 5 — Boston, MA

- 3-day 275 mile bike ride, personally raised over $2500 — 1999

RENSSELAER POLYTECHNIC INSTITUTE — Troy, NY

- Varsity Soccer, Most dedicated, UCAA All-Academic team, Captain — 1993-1996
- Varsity Basketball — 1993-1994
- Varsity Lacrosse — 1995-1996

Patents and Publications

Kerdok, A. E., R. D. Howe, 2003, "A Technique for Measuring Mechanical Properties of Perfused Solid Organs," ASME Summer Bioengineering Conference, Key Biscayne, FL.

Kerdok, A. E. *et al.*, In Press 2003, "Truth Cube: Establishing Physical Standards for Real Time Soft Tissue Simulation," *Medical Image Analysis*.

Walczyk, D. F., A. E. Kerdok. (Rensselaer Polytechnic Institute, 2002) pp. US 6,405,606 B1.

Kerdok, A. E. *et al.*, 2001, "Truth Cube: Establishing Physical Standards for Real Time Soft Tissue Simulation," International Workshop on Deformable Modeling and Soft Tissue Simulation, E. Keeve, Bonn, Germany.

Kerdok, A. E., A. A. Biewener, T. A. McMahon, P. G. Weyand, H. M. Herr, 2002, "Energetics and Mechanics of Human Running on Surfaces of Different Stiffnesses," *Journal of Applied Physiology* Vol. **92**, pp. 469-478.

Kerdok AE, "Energetics and Mechanics of Humans Running on Surfaces of Difference Compliance," M.S. Thesis, Mechanical Engineering Dept. Massachusetts Institute of Technology, September 1999.

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EDUCATION

Ph.D. in Biomedical Engineering — **Harvard University**
Division of Engineering and Applied Sciences — Defended August 2003
Harvard Biorobotics Laboratory — Expected Completion November 2003

Master's degree in Engineering Sciences — **Harvard University**
Division of Engineering and Applied Sciences — October 2002

Master's degree in Engineering — **Massachusetts Institute of Technology**
Electrical Engineering — September 1999
MIT Sea Grant Autonomous Underwater Vehicles Laboratory

Bachelor of Applied Science, Biomedical Engineering — **University of Toronto**
Engineering Sciences — May 1997
Graduated with Honours, first in class

RESEARCH EXPERIENCE

Sept '99 – present
Research Fellow at Harvard BioRobotics Laboratory — **Cambridge, MA**
- Developed clinical studies in concert with surgeons and radiologists
- Analyzed and compared physiological signals and finite element data
- Supervised undergraduate assistants

January '00 - June '01
Research Consultant at Assurance Medical — **Hopkinton, MA**
- Assessed performance of sensors and effects of calibration
- Analyzed clinical trial data

Aug '98 - Aug '99
Research Engineer at Webb Research Corporation — **Falmouth, MA**
- Developed high level control program and dynamic simulator for gliding autonomous underwater vehicles
- Responsible for land operations in autonomous vehicle confined water testing

Sept '97 - Aug '99
Research Assistant at MIT Sea Grant — **Cambridge, MA**
- Developed simulation for slow, long-range underwater glider vehicles in high currents
- Assisted in vehicle configuration design and power consumption analysis

May '96 - April '97
Research Assistant at Computer Integrated Manufacturing Lab, University of Toronto — **Toronto, ON**
- Designed and implemented sensory circuitry for automatic calibration of robotic system
- Responsible for assessing stereolithography system parameters

May '95 - August '95
Research Assistant in Clinical Engineering, University of New Brunswick — **Fredericton, NB**
- Analyzed hospital ICU data for neural network project
- Advised on second year electrical engineering curriculum
- Assisted in organizing a national Women in Engineering Conference

TEACHING EXPERIENCE

September 2000 - present
Fencing teacher and coach, invited to teach at world-wide conference on rapier studies
August 2002 - present
Teacher of historic metalcasting techniques
September - December 2002
Teaching Consultant in Training, Derek Bok Center for Teaching and Learning
Spetember - December 2001
Teaching Fellow for Harvard Systems Analysis with Physiological Applications class
January - May 2000
Teaching Fellow for Harvard Partial Differential Equations and Vector Calculus class
1987 - 2002
Private tutor in various subjects to students from the elementary to university levels
2000 - 2002
Mentor to middle-school children, guest lecturer on various engineering subjects
1991 - 1993, 2001-2002
Teacher of piano to children and adults
1990 - 1993, 1997
Guest lecturer of cartooning, art and origami at Elementary School Gifted Students Mentorship Days

SELECT ACHIEVEMENTS

- Winner of UUST (Unmanned Untethered Submersible Technology) Student Paper Competition 1999
- Finalist in MasterWorks '99, a competition for MIT Masters theses 1999
- Unanimous winner of University Scholarships Canada award for Graduate Studies 1997
- Received Irving Krausmitz award for excellence in Biomedical Engineering 1997
- Awarded the Canadian Engineering Memorial Foundation final year undergraduate scholarship 1997
- Recipient of SCIEX Award for excellence in Instrumentation Design 1997
- Recipient of AECL Research Award 1997

PUBLICATIONS

Kerdok AE, Cotin SM, Ottensmeyer MP, Galea AM, Howe RD, Dawson SL. *Truth Cube:Establishing Physical Standards for Soft Tissue Simulation.* Medical Image Analysis, September 2003.

Galea, AM, Howe RD, *Mammography Registered Tactile Imaging.* IS4TM 2003 Juan-Les-Pins, France, June 2003. Springer-Verlag LNCS 2673, Berlin. pp183-193, 2003

Galea, AM, Howe RD, *Tissue Stiffness from Tactile Imaging.* IEEE Eng. In Med. and Bio. Soc. Houston, October 2002.

Kerdok AE, Cotin SM, Ottensmeyer MP, Galea AM, Howe RD, Dawson SL. *Truth Cube:Establishing Physical Standards for Real Time Soft Tissue Simulation.* Int. Workshop on Deformable Modeling and Soft Tissue Simulation. Bonn, Germany, November 2001.

Galea AM, Dennerlein JT, *Schlager Fencing Biomechanics: Determinates of Impact Force.* American Society of Biomechanics. Chicago, July 2000.

Galea AM, *Various methods for obtaining the optimal path for a glider vehicle in shallow water and high currents.* Proc. 11th Int. Symp. Unmanned Untethered Submersible Technology. New Hampshire, August 1999.

Galea, AM. *Mapping Tactile Imaging Information: Parameter Estimation and Deformable Registration.* Division of Eng and App Sci, Harvard University, Cambridge, 2003

Galea, AM. *Optimal Path Planning for Glider Vehicles in Shallow Water and High Currents.* Department of Elec Eng and Comp Sci, MIT, Cambridge 1999

Galea, AM. *Stereolithography System Parameter Identification.* Division of Eng Sci, Univ of Toronto, 1997

In Preparation

Tissue Parameter Extraction from Tactile Scanning: IEEE Trans. Medical Imaging.

Mammography Registered Tactile Imaging: Medical Image Analysis (MedIA).